American Journal of Obstetrics and Gynecology

VOL. XXV ST. LOUIS, JANUARY, 1933 No. 1

Original Communications

THE COMPLICATIONS OF RADIUM THERAPY IN GYNECOLOGY*

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(From the Clinic of the Woman's Hospital)

THAT facilities to treat cancer patients must be established in our general hospitals throughout the country as well as in the large special institutions such as the great cancer clinics of Stockholm, Paris, Munich, and New York, is inevitable, because the patients suffering from cancer are already far too numerous for these centers to take care of and the disease is steadily increasing.

This means the staff of the general hospital must be educated to a proper appreciation of the complexities of this disease, and must be trained in the most approved technic of radium therapy as well as surgery, for without this agent available no hospital today can be considered properly equipped.

On superficial thought the acquiring of this knowledge and technic of radium therapy seems a comparatively easy matter as the application of the element appears so simple. The alluring advertisements of the commercial agencies who rent radium, urging the general practitioner to send a description of the case, and they will forward directions with the proper dosage of radium, apparently confirms the prevailing impression that any one can apply it without special knowledge or skill.

Let me emphasize the warning of Madame Curie on her last visit to this country when she called attention to the great dangers of the improper use of radium. As Regaud, of the Paris Clinic, has recently said, "It is necessary to have much experience to obtain from this method of treatment all the good that it may give without the evil that it may do."

"Correspondence Courses" in radium therapy are dangerous for the

*Read at a meeting of the Brooklyn Gynecological Society, May 6, 1932.

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inexperienced. While the renting of radium from these agencies is of course perfectly justifiable, the knowledge and judgment as to how and when to use it can only be bought by careful study and personal experience and observation in radiologic clinics. Indeed radium is a two edged sword, and its use is far from simple.

To appreciate this we must first have some knowledge of the action of radium on the tissues. Radium does not remove a cancerous growth by destruction of the entire part affected as is accomplished by surgery or cautery, but the gamma rays have a direct selective action on the cancer cells, destroying them without injuring the normal cells at the site of the neoplasm.

This is demonstrated in healed cases of carcinoma of the cervix, where the normal shape of that organ may be restored with no trace of the site of the growth.

Another action of radium is to cause the proliferation of connective tissue. The connective tissue contracts, with the resulting obliteration in great degree of the blood and lymph supply, producing the contracted, pale looking cervix and funnel shaped vaginal vault, that we see in the ideally healed cases.

If the dosage suitable for a certain case is used, we will destroy the cancer cells but *not* the normal tissues, owing to the selective action of the gamma rays on the carcinoma, and the greater resistance or toleration of the normal tissues.

If we give much larger doses of radium than is required to destroy the cancer cells, we will also destroy the normal structures and produce extensive necrosis with its resulting septic absorption, hemorrhages, and injury of adjacent viscera, with perhaps the production of fistulas.

Remember also that these unfortunate results of overradiation with this powerful element are commonly attributed to the extension of the carcinoma, or frequently the action of the radium is blamed and consequently condemned as of no value.

We must see also that if too small an amount of radium is used, or for too short a time, that we may fail to destroy all the cancerous tissue.

Upon the proper screening of the radium depends the elimination of the beta, or burning rays, which cause extensive destruction of the normal tissue. Various metal containers of different thickness are used such as platinum, gold, silver, or brass for this purpose, and damage of the bladder and rectum is avoided by "distance screening," that is pushing them out of reach of the rays by overdistending the vagina with gauze. If inadequate screening has been used, unnecessary necrosis will result.

Too frequently repeated radiations, especially if a heavy dosage for prolonged periods is employed, will result in the so-called "late reaction" of radium. Six months, or a year or more, following the initial treatment dense infiltration, pelvic pain, ulceration, and discharge may develop, which is apt to be attributed to a *recurrence* of the disease, when

actually it is the result of an overirradiation of the tissues with a resulting excess of connective tissue formation. This produces a slowly developing obliteration arteritis, and the devitalized structures ulcerate and become a ready prey to infection.

From this brief summary of the action of radium on the tissues and the damage that it may cause by a defective technic, it should be appreciated that safety in its use depends on the *careful study* of the *location* and *extent* of the disease, of the *type of cell* and the *degree of its maturity,* of the *general physical state* of the *patient* as to *age, blood condition,* and *toxemia,* of the *careful preoperative preparation* of the patient, of the *amount* of *radium used* and its *distribution* in *appropriate containers,* on the *proper employment* of *screening* to *cut out the burning rays,* on the *placing* and *maintaining* of the *radium in situ* where it will destroy the cancer and yet not damage adjacent viscera, on the *duration* of the application, and the *time* and *dosage* of *reradiations* and *deep x-ray therapy,* and finally on a *careful frequent follow-up.*

A personal experience in studying the action of radium on this disease over considerable periods of time is essential before one can become competent to properly treat cancer of the uterus with radiotherapy.

The complications that we may encounter in radiotherapy of the uterus are many. Some of them we cannot avoid, but the incidence can be materially reduced by following the accepted technic of those experienced in its use.

It is of interest to note that in the enormous mass of literature that has been published on radium therapy, while the complications are mentioned, it is rare to find a detailed analysis of the subject.

Very little has been written regarding the frequency of postradiation symptoms, yet as they are encountered in all clinics, varying from mild temporary discomforts to severe and most distressing complications, involving prolonged suffering and even death, it would seem of value to study this phase of radium therapy in the hope of reducing their incidence.

We have recently had an analysis made of 558 cases of carcinoma of the cervix in our clinic, and there were 119 who had some form of postradiation morbidity, or 21.3 per cent.

In 106 cases of carcinoma of the fundus, of which 88 were treated by radium, 11.4 per cent had complications.

This study shows that there has been a gradual decline in the frequency of complications in the latter years in this series. This is probably due to the more meticulous attention paid to the details of the technic and to an improvement in judgment as a result of our experience.

The primary mortality from radium therapy in carcinoma of the cervix should not exceed 2 per cent. It should be nil in the early cases (Class I and Class II). In our last published series it was 1.1 per cent, with none for the Class I and II cases. This mortality is nearly always

due to the unwise employment of radium in cases with extensive disease in which an acute sepsis is present or results.

When the destroyed carcinomatous tissue sloughs away as a result of the action of the radium, a certain amount of bleeding (secondary hemorrhage) will occur in some cases, which varies in amount from a moderate oozing to a severe hemorrhage in those cases where the disease has encroached upon the blood vessels, and may require prompt packing.

In our series we have had some bleeding in about 10 per cent, but very few were of the severe type.

Vesical irritability and rectal irritability as a result of the action of the rays on the bladder and rectum is mentioned as a frequent complication by many clinics.

In our hands we have had comparatively few cases where this has been troublesome, approximately 4.5 per cent.

We believe that this is due to the meticulous care we use in distending the vagina to the utmost with gauze packing, thus getting the maximum value of "distance screening."

As we have observed the technic in some clinics this extreme distention of the vagina is not always done.

We believe also that the use of a self retaining catheter in the bladder while the radium is in place, helps by keeping the bladder collapsed, as the full bladder lies close to the anterior uterine wall and the radium in the uterine cavity, which has a penetration of about 3.5 cm., can easily reach the bladder.

Radiation cystitis is manifested by frequency and dysuria, and may be very troublesome and last for a long time, as ulcerations may result.

Proctitis is evidenced by diarrhea, rectal pain and ulcerations. Our incidence was 3.1 per cent. Most writers speak of this as a more troublesome complication than cystitis.

These ulcerations of the bladder and rectum are often mistaken for an extension of the carcinoma.

Vesicovaginal fistula is one of the most distressing complications that we meet in radium therapy. It is frequently difficult to tell whether the fistula is a result of the extension of the disease or of the radiation. Should the disease invade the anterior vaginal wall, there is great danger that a fistula may be produced if the dosage is too large.

Judgment as to the proper dose must be based on the thickness of the septum and upon experience.

I believe one of the most dangerous conditions we have to deal with is in those cases where a previous supravaginal hysterectomy has been done and cancer has developed in the cervical stump.

The bladder then lies on top of the cervix at the site of the amputation where it will come in direct contact with the radium tube placed in the cervical canal.

We have seen 40 cases of cervical carcinoma which had had a previous

hysterectomy in our series of 558 cases, or 7.2 per cent. Some of these developed a fistula, whether from the radiation or the disease we are not sure. In these patients the incidence of hemorrhage was increased one and one-half times, and of fistula two and one-half times, so in recent years it has been my practice to reduce the radiation one-half in these cases, repeating as necessary.

Vesicovaginal fistulas do not tend to heal of themselves. In two instances I have successfully closed these postradiation fistulas by operation.

CASE 1.—Miss M. J., aged thirty, came under my observation in February, 1927, with carcinoma of cervix Class III, squamous cell Group I. She was given 4200 mg. hours. She had considerable slough and did not respond well, became cachectic, lost weight and developed a vesicovaginal fistula in the anterior vaginal vault 2 cm. in diameter. She entered the House of Calvary as a hopeless case, but to our astonishment returned to our follow-up clinic in December, 1927, with no evidence of the disease and feeling perfectly well except for the fistula. I successfully operated upon her in February, 1928, and she has remained in excellent health to date.

CASE 2.—Mrs. M. S., aged forty-three, had had an amputation of the cervix followed by radium therapy for carcinoma in a neighboring city in November, 1927. She came to the Woman's Hospital in January, 1929, suffering from a vesicovaginal fistula in the vault and dense infiltration of the entire anterior vaginal wall and a severe cystitis. She was thought to have a metastatic invasion of the bladder and seemed a hopeless case. On passing a sound into the bladder, a click demonstrated the presence of a large calculus which was firmly imbedded in the trigone and which gave the impression of a dense infiltration. I did a cystotomy from above, removed the stone and drained; the bladder promptly cleared up, and she rapidly recovered with no evidence of carcinoma. The fistula I attempted to close in May, 1930, but failed. It was an exceedingly difficult case owing to a small contracted vagina and dense scar tissue forming the margins of the fistula. I tried again in February, 1931, with the same result. In December, 1931, a third attempt was perfectly successful. I succeeded this time because I first dissected out the entire funnel shaped vault of postradiation scar tissue, in the apex of which was the fistula.

Rectovaginal fistulas sometimes heal of themselves, but the most troublesome cases are those which develop an ileovaginal fistula. On account of the liquid state of the stools, which are intensely irritating, these patients suffer excruciatingly. This complication may be caused by a loop of the small intestine being adherent in the culdesac or to the posterior surface of the uterus, and excessive radiation or the extension of the disease results in the fistula. We had such a case due to the extension of the disease as proved by autopsy, in which three loops of small intestine were adherent to the back of the uterus and culdesac.

The most unusual case of rectovaginal fistula we have encountered was as follows:

Mrs. E. O., aged twenty-seven, came to the clinic in July, 1926, with a carcinoma of the cervix Class III, Group I. She was radiated but did not respond well, and as she seemed in a hopeless condition entered the House of Calvary in January, 1927. She returned to us in September, 1927, apparently free from carcinoma. In February, 1930, she developed a pelvic abscess which resulted in a fecal fistula between the upper sigmoid and the vaginal vault. The fistula, however, was small and did

not trouble her greatly unless her bowels were loose. In February, 1932, she developed an acute cellulitis over the center of the posterior surface of the sacrum which we felt certain was due to bony metastasis, although the x-rays were negative. On March 8, 1932, I opened this abscess and the next day a fecal discharge was in evidence. X-ray studies showed that this sinus ran through the sacrosciatic notch to the original fistula which thus discharged through the vagina and through the back over the sacrum. On March 29, 1932, I made a temporary colostomy and the sacral sinus has closed and the vaginal sinus nearly so. There is no evidence of carcinoma to be determined and she seems perfectly well nearly six years after her original radiation. It is our intention to close the colostomy should the vaginal fistula heal.

There were 22 cases of fistulas in our series of 558 cases, or 4 per cent. What proportion were due to the radiation and what to the disease it is not possible for us to determine.

We believe that cases having a history of previous pelvic inflammatory disease with or without operation are liable to intestinal fistula as a complication of the treatment or the disease on account of the proximity of an adherent loop of bowel to the site of the disease.

As a result of the contraction which follows radiation, due to formation of dense connective tissue, the cervical canal may be partially or completely occluded. An infection of the endometrium of the uterine cavity frequently results, and a condition of pyometra develops with or without retention. Cramplike pains due to uterine contractions and enlargement and softening of the fundus are suggestive signs.

A monthly follow-up of all cancer cases such as we have at the Woman's Hospital enables one to discover this complication in its incipiency, and the passage of a sound makes the diagnosis and corrects the condition.

Pyometra was a complication in 3.6 per cent of our series.

The primary mortality in radium therapy is almost always due to the lighting up of a septic infection which results in peritonitis. The carcinomatous cervix with its sloughing and ulcerated surface is likely to harbor pathogenic bacteria. Preliminary vaginal antiseptic douching should be employed. Trauma in dilating the cervix and placing the radium should be avoided. A biopsy is safest when done with the radio knife. The presence of a temperature and signs of pelvic inflammatory disease should indicate rest in bed for a few days as a preliminary measure.

Anemia and asthenia should be combated with a blood transfusion prior to the radiation.

A temperature reaction up to 101° may be considered as normal immediately following the application of radium, but it should promptly subside. High temperature after radium therapy was formerly attributed to the absorption of toxic substances from the disintegrating tumor, but it is now known to be from infection. We are inclined to believe that the high incidence of sepsis following radiations in some clinics may be due to the daily and repeated intrauterine applications.

In our clinic the incidence of sepsis as indicated by a temperature of 102° or more is but 2.7 per cent.

The contraindications to radium therapy are few, except in cases with an active septic infection and peritonitis, and in advanced Class IV cases with frozen pelvis.

Sloughing ulcer from over irradiation and insufficient screening, which means destruction of normal tissues as well as the carcinoma, should be preventable.

Late reactions coming on six months or a year after the initial treatment and which are frequently mistaken for a recurrence of the disease are likewise usually due to over radiation.

Radium burns in normal tissue from displacement of the radium is apt to occur if the applicators are not anchored in place. We believe this is an important point in the technic of application as shown in the following case:

Mrs. S. had had radium and x-ray therapy for nonmalignant metrorrhagia. She came to me three months later suffering excruciating pain in her vagina and a foul discharge. Examination disclosed a sloughing ulcer in the right lateral vaginal fornix the size of a quarter with acute vaginitis and infiltration. The possibility of malignancy was considered but a biopsy proved there was no malignancy. The ulcer was evidently due to a radium burn from the applicator becoming displaced alongside the cervix. After five months of suffering the ulcer entirely healed with complete relief from pain.

Nausea and vomiting occasionally occurs while the radium is in place but was noted in less than 1 per cent of our cases.

The contraction of connective tissue formation in the broad ligaments is a late complication and may produce an obstructed ureter and involvement of the kidney. Severe deep seated pelvic pain, if not due to the disease, is probably the result of connective tissue contraction. Stricture of the urethra also has been observed.

Phlebitis involving the leg may occur. We encountered it in 0.54 per cent.

In the 106 cases of carcinoma of the fundus we have encountered, 88 were treated by radium therapy, either alone or in combination with surgery. We prefer to give an intrauterine application of radium at the time of the diagnostic curettage in these cases followed by a panhysterectomy four weeks later. In about 50 per cent of these patients we have been compelled to use radiotherapy alone because they were poor operative risks. These fundus cases were less apt to have complications than the cervix cases, as there were twice as many complications in the latter. It is noteworthy that postradiation hemorrhage did not occur at all in the fundus cases, while pyometra was more frequent, being met with in 4.6 per cent as compared to 3.6 per cent in cervix carcinoma.

As we would expect, proctitis is one-third less frequent than in the cervix patient.

One of the most distressing complications we can encounter from radium therapy is when it is used to check a menorrhagia in a young woman and an overdose is given.

In such intractable bleeding cases which do not yield to curettage or hormone therapy success may be achieved with a very small dose of radium, 200 to 400 mg. hours. If we approach 600 mg. hours we are in danger of causing a permanent amenorrhea and atrophy.

It is far better to underradiate these cases with the understanding that the treatment may have to be repeated, than to give too much.

Miss V. R., aged twenty-five, and socially prominent, was brought to me by her mother for an amenorrhea of one year's duration and menopause symptoms following an intrauterine application of radium for a persistent menorrhagia which had not been relieved by repeated curettage. The examination disclosed an atrophic uterus with a contracted canal. On inquiry, her physician stated to me that he had called in a radiologist who had given the patient a dosage of 1440 mg. hours. She was of course beyond relief, and as she wished to get married the family were greatly distressed.

I know of a similar instance of an inexcusable over dosage in a young girl.

CONCLUSIONS

Since 1919 to date we have had in our cancer clinic some 560 cases of carcinoma of the cervix and 106 cases of fundus carcinoma.

A study of these cases shows that approximately 19 per cent have had some form of complication, although the large majority have been of a minor and transitory type.

We cannot always avoid some of these complications as they occur in the most experienced hands, but they can be materially reduced in number, if the action of radium on the tissues is understood and meticulous care is taken in following the essential details of the preliminary treatment and technic of application.

It is just as necessary that men should be properly trained in the treatment of cancer of the uterus by radium therapy, if satisfactory results are to be obtained, as that they should be properly trained in surgery.

As Lord Moynihan has stated, "The surgeon's knife in most highly trained hands is an instrument of great delicacy, but it cannot always discriminate between healthy and diseased tissues. Radium is an instrument of far greater delicacy because its action is selective, that is to say, it acts differently upon diseased and healthy tissues, killing one and leaving the other."

Finally I desire to emphasize the fact that the safe employment of radium requires experienced piloting as we are literally sailing between Scylla and Charybdis in attempting to avoid the damage we may inflict by overradiation on the one hand and the failure to destroy the disease by insufficient radiation on the other.

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DISCUSSION

DR. HARVEY B. MATTHEWS.—Complications, both severe and mild, are known to follow the use of radium, but very few of us have taken the trouble to tabulate our cases as Dr. Ward has done in an effort to ascertain the complications that actually occur. Dr. Ward has tabulated every complication except perhaps one, a severe vaginitis, very intractable, causing considerable disability, but after a long period of treatment, finally healing.

The late complications including the indurated cicatricial scars in the broad ligaments, are not always due to irradiation, but are aggravated by it and become more solidified, almost cartilaginous in character. It is no wonder that they produce very severe, disintegrating, continuous pain. If the ureter is in the scar, then we have superimposed the symptoms caused by this complication.

Dr. Ward did well to insist that this work needs special training. Experience is required not only in the treatment of the cervical and body cancer cases, but the nonmalignant uterine bleedings as well.

DR. WILLIAM SIDNEY SMITH.—We use radium at the Brooklyn Hospital very similarly to the manner in which Dr. Ward uses it. Our service is small. I would like to urge the value of heavily screened radium and that you are much less likely to get into difficulties than if you use radium screened so that the Beta rays get through. We use radium screened with a full millimeter of platinum and have had but few bladder complications (cystitis, etc.) and very few rectal complications, than elsewhere, because in early carcinoma of the cervix we almost always use it in conjunction with cautery. If the case is early, and the cervix can be pulled down, we do a Byrne cautery operation and then put the radium in the cavity. If the case is farther advanced, with some induration, and the cervix will not come down, we often sear off the sloughing mass with the cautery and then insert the radium, either in the form of a T with one capsule within the remainder of the cervix and the other crosswise against it, or we use both capsules in parallel right up against the cervix. It is interesting to note that our only bladder fistulas have followed operations in which the cautery was used. In one case in which a Byrne cautery operation was done radium was inserted for 2,400 hours, the patient was sent for x-ray and she was given heavy x-ray dosage which, by the way, caused a great deal of shock. In two months we gave her another dose of radium (2,400 hours) and the x-ray was again tried, but the shock was so great she was only given one dose. That was nine years ago. She is still alive, but has had a bladder fistula for five years. There is a great deal of induration in her pelvis and very little mobility. I have advised her against trying to have the fistula repaired because I think it might light up her carcinoma. She gets along fairly well with it.

The other fistula occurred after a cautery amputation of a carcinoma of the cervix with the radium laid against it. Her carcinoma seemed to be fairly well healed for a time, then the fistula developed. It was closed by operation for about six months, and then broke down, the carcinoma lighted up, and she finally died.

DR. DAVID FEINER.—The mischief that can follow the improper introduction of radium, is shown by a case of a woman who was in labor at home for about twelve hours under the care of a midwife. When brought in the cervix was three fingers' dilated, the cord prolapsed and a foot protruded. A physician was called in who did not recognize the pathology that was present and tried to do an extraction. The patient was about seven months pregnant. He thought the child was undersized and would come out without much difficulty. He desisted after he had removed the body up to the neck, and the latter snapped, with the head remaining inside. I then saw the patient and found a dense cicatricial stenosis of the cervix with marked fibrous replacement of the entire vault of the vagina. The head was oversized, ap-

parently hydrocephalic. We tried to incise the cervix and made very little progress because of the severe bleeding. We finally did a laparotomy and removed the uterus with the contained head. On subsequent inspection of the uterus and microscopic examination of the sections of the lower segment the cervical portion showed extensive fibrous replacement of the muscle tissue and undoubtedly in this case in which radium had been used, the cavity of the uterus was not packed to keep the tube up near the fundus where it belonged, but was allowed to prolapse down to the cervical canal and brought about cicatrization and stenosis.

DR. GEORGE G. WARD.—Vaginitis may occur, although we have had very little difficulty with that complication, In one instance there was definite sloughing of the vaginal mucosa which caused a good deal of trouble. I have always felt that the marked distention of the vagina with gauze was a preventive.

As for involvement of the bladder, it is not uncommon in our experience when we send a case to the urologic department to have a report that there is metastasis in that organ. In quite a number of instances this has proved not to be the case, but a bullous edema and possible ulceration was there, due, undoubtedly, to the radiation. Those cases have in a number of instances entirely cleared up although they have a prolonged convalescence. We must not immediately jump to the conclusion that it is carcinoma of the bladder, and must remember that it may be due to the radium.

For a long time I feared that the repair of a postradiation fistula might light up latent cancer cells imprisoned in the connective tissue. Our pathologist examined all tissue removed in cases of vesicovaginal fistula and in no case were carcinoma cells found in the cicatricial tissue around the fistula.

The difficulty of removing radium is an important matter and that is why we have developed the particular technic employed. The displacement of a tube of radium from the canal is due to the contraction of the uterus. That is why we anchor the radium in place.

THE TECHNIC OF RADIATION THERAPY IN UTERINE CARCINOMAS*

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THE criteria of an adequate radiation tissue dose delivered into a deep seated or internal carcinoma are a rapid resolution of the growth, a restoration of the surface epithelium and a limited fibrosis. The predetermined radiation tissue dose evidently should be uniformly or homogeneously distributed throughout the cancer bearing area. The radiation dose should be lethal to the carcinoma cells and should not cause irreparable injury to the normal tissue lying within the radiation field.

The good end-results depend not only on an adequate, homogeneous radiation tissue dose but also on the location of the growth, on the clinical extent of the tumor, the degree or grade of histologic malignancy, the presence of complicating infections and the general constitutional state of the patient as determined by age, cachexia, toxemia, complicating diseases, etc. These factors are only mentioned since the following discussion is limited to the technic of radiation therapy.

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*Read at a meeting of the Chicago Gynecological Society, February 19, 1932.

The lethal radiation tissue dose for sarcomas and carcinomas has been tentatively placed by Wood and Prime[1] at about 4.5 to 7 erythema doses of filtered roentgen rays or gamma rays applied to the tumor. The tumor should be rapidly growing, very cellular and highly malignant. These are characteristics associated with a high degree of radiation sensibility. Wood[2] further states that the production of absolute permanence of cure by radiation therapy implies that the destruction of the tumor cells must be as complete as must be their removal for effective surgery. These findings have been corroborated by clinical experiences as reported by Quick,[3] Lee,[4] Pfahler,[5] Schmitz,[6] and others.

The radiation tissue dose for highly cellular and highly anaplastic undifferentiated carcinomas of the uterus is probably 4 to 5 erythema doses according to our observations. It is necessary to apply this intensity uniformly throughout the true pelvic cavity. The methods employed to accomplish this will be described in the following discussion.

PHYSICAL PRINCIPLES OF DEEP IRRADIATION THERAPY

The physical principles of the production of x-rays and radium must be known in order to obtain the best results in the treatment of malignant diseases by radiation. It was deemed desirable therefore to discuss some facts of a rather technical nature such as the methods of application of radiations, the relation of the time duration of radiation to the total dose, the factors to be observed and to be recorded on the treatment charts, and the definitions of the erythema dose, designated E. D. and of the international roentgen dose unit designated "r."

Radiations may be applied cavitarily, interstitially or distantly. The insertion of radium into the cervical canal or the uterine cavity is a cavitary application. The introduction of the needles containing radium or radon into the tumor, as in the pallisading of the cervix or paracervical tissue, is an interstitial method. The application of roentgen rays or of radium contained in a so-called cannon is a distant method.

The time duration within which a complete radiation series is given may vary. The application of the full dose may be done within the shortest possible space of time. This single "massive intensive" method is advocated for roentgen rays by Kroenig and Gauss,[7] and Seitz and Wintz,[8] and for radium by Kelly and Burnam,[9] Healy[10] and others. The tolerance tissue dose, that is the highest dose tolerated by normal tissues without serious primary injuries is applied in a single continuous sitting, the dose being about 250 per cent E. D. Additional radiations are not advisable. If reradiation is necessary then a decreased dose may be applied six to twelve weeks later. It is a well established axiom that the first course of radiation treatment should be applied in such adequate doses that the growth will be arrested, since radiations added at a later time are as a rule ineffective.

An erythema dose may be given at once and followed by the additions of smaller doses at stated intervals of three to seven days until a total

dose of 2 to 2.5 E. D. has been attained. In this way the radiation effect is maintained at full saturation. It is known that the loss of radiation effect of the short wave radiations used in deep cancers amounts to 4 per cent daily; hence 12 per cent of an erythema dose may be added every third day, or 25 per cent of an erythema dose every seven days until a total dose of 2 to 2.5 E. D. has been given. The "saturation" method was introduced by Pfahler[11] who based the observation on earlier data of Kingery.

A fraction of a dose, for instance, 40 per cent of an erythema dose may be applied every third day 5 times, or 30 per cent of an erythema dose may be given every third day 10 times. In other words the *fractional* dose is *scattered* over fifteen to thirty days. The *scattered fraction* method has been employed in our clinic for the last twelve years. In Europe it is known as the Coutard protracted fractional method.

In the Coutard method small ampere loads are used so the single treatment is applied within an hour, i. e., it is protracted. We use loads of 25 to 30 milliamperes and the application of each fractionated dose lasts from ten to fifteen minutes depending on size of filter and focus skin distance.

The advantages of the scattered fraction method are: (1) Large total doses can be applied without permanent injury to the normal structures. The total dose may be from two to three erythema doses. (2) The cancer cell is hit by the rays during the most radiosensitive stage which is the time of mitoses occurring in highly undifferentiated embryonal cells about every six hours and in more mature cells about every twelve days. This is also known as the karyokinetic index of Proust and de Nabias which is based on the ratio of the number of mitotic to the number of resting cells. The lower the index the lower is the radiosensitiveness of tumors and the more protracted the treatment should be. If the ratio is 1 mitosis to 50 to 100 resting cells then the treatment should last six days. Should the ratio be 1:100 to 1:150 the treatment should be extended to fourteen days; and should the ratio be 1:150 or less, then the treatment should last for twenty-five to thirty days. (3) Normal tissues react with a mild fibrosis, a desirable attainment as it means the production of a defensive and phagocytic tissue.

A radiation dose is the product of intensity and time. In order to correctly describe a radiation technic it is necessary to state the factors used in the application. They are: (1) location of tumor; (2) size of tumor; (3) depth of tumor; (4) strength of radioactive source; (5) distribution of radioactive source; (6) filtration; (7) distance or spacing; and (8) duration of application. To determine the location, the size and the depth of a tumor a caliper and a modified pelvimeter are used. The outline and the circumference of the body are drawn on tracing linen and the size and depth of the tumor from the anterior abdominal wall as measured with the pelvimeter are entered (see Fig. 1).

The strength of the radioactive source should be stated in milligram radium element hours or in millicurie radon hours with allowance for decay. The distribution of the radioactive source should describe the construction, the shape and the dimensions of the applicator as tube or plaque used for the application. The effective length of distribution of the radioactive material in tubes or needles should be given. The filtration should designate all of the materials interposed between the radioactive substance and the tumor including kind and thickness of the metal, rubber, leather or paraffin filters and the approximate thickness of the tissues from the surface to the tumor.

Distance is one of the most important factors in radiation therapy. It should be measured from the center of the source to the surface of the tissue or skin. In interstitial radiation it is important to state the spacing. Hence the number of needles or implants, the strength of each, the

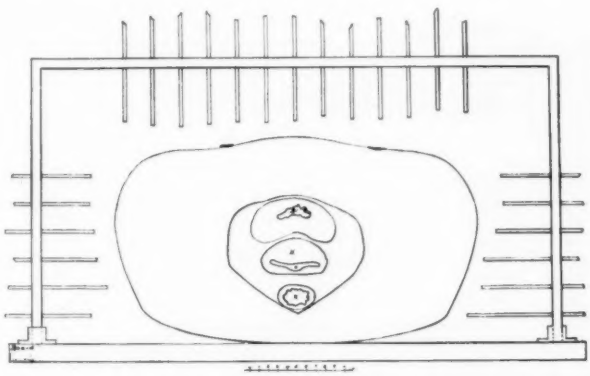

Fig. 1.—Caliper to obtain the outline of the pelvis. Location of the uterus is determined by a modified pelvimeter, one arm being straight and flexible to obtain depths and direction of uterine canal.

length of active surface, and the thickness and kind of metal container should be recorded. If cross firing be used then the location, the size of the fields and the focus skin distance should be recorded by means of a diagram. Lastly the duration of each seance with the interval between each should be given and each recorded separately. The total dosage of gamma rays *may* be expressed in milligram element hours if all the factors are otherwise given.

The factors in roentgen ray therapy include the source and type of generator and tube, the wave length, the kilovoltage, the milliamperage, the size and location of fields, filtration, the focus skin distance and the duration and date of each treatment.

The total dose should be expressed in values of E. D. or "r" units, and the time within which it is applied should be stated. If the x-rays are used, the quality of radiation as determined by the wave length should be recorded. It is not necessary to specify the wave length of radium as this is constant and equals a minimum wave length of 0.011 A. U. or

1128 K. V. according to Thibaud, and an effective wave length of 0.022 A. U. or 600 K. V.

The threshold erythema dose is defined as the amount of radiation which, if delivered in one sitting, will in 80 per cent of the cases treated produce a faint bronzing or reddening of the skin and in the other 20 per cent of the cases will produce no visible effect.[14] The erythema dose therefore is based on a biologic reaction namely the bronzing or reddening of the squamous cell epithelium of the skin.

The international roentgen unit "r" is the quantity of roentgen radiation which when the secondary electrons are fully utilized and the wall effect of the chamber is avoided produces in 1 c.c. of atmospheric air at 0° C. and 76 cm. mercury pressure, such a degree of conductivity that one electrostatic unit of charge is measured at saturation current.[15] It is purely a physical measurement. However, E. D. may be expressed in terms of r. One E. D. is 600 r measured on the body surface. The tolerance E. D. means the highest dose that may be applied to the skin in one sitting and is about 250 per cent higher than a threshold E. D.

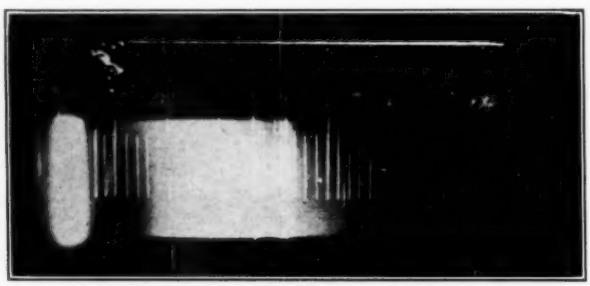

Fig. 2.—Spectrographic measurements of x-rays produced with the factors 200 K. V. and 0.75 mm. copper and 1.0 mm. aluminum filter. Shortest wave length is 0.067 A. U.; longest wave length 0.27 A. U.; average wave length 0.15 A. U.

Dosimeters standardized in r are used to determine the output of x-rays from a tube so that the time duration can be calculated within which a known amount of r may be applied.

The scattered fraction method which has been used in our clinic for about twelve years permits the application of doses that could not be made with any other technic. If one uses 200 kilovolts, a focus skin distance of 65 to 80 cm., a filter of 0.1 mm. copper plus 0.1 mm. aluminum, and a field size of 300 to 420 cm.^{2} then one may apply a roentgen dose of 240 r every third day for 5 times, i. e. a total dose of 2.0 E. D. or 1200 r given within fifteen to eighteen days. If applied in 180 r doses then 10 times 180 r may be given within twenty-seven days. The skin will show an intense erythema after two weeks and a desquamation of the superficial layers of the skin within another eight days. The latter will heal readily within two weeks.

The gamma rays of radium have been measured by Glasser and Mautz in r units and they showed the erythema dose of gamma rays of radium to be 2000 r. Accordingly a 50 milligram element radium capsule in-

serted intracorporally into the cervical canal for 4800 mg. el. hr. will give at a distance of 4 cm. 2500 r and at 5 cm. 1450 r. The intensities measured in r may therefore be determined by the equal intensity curves. Should the determinations of r values of gamma rays by Glasser and Mautz be correct then our values for isodoses 5 and 2½ will have to be corrected. Instead of 25 per cent E. D. or 500 r at isodose 2.5 the value in r would be about 667 r as 2000 r measured with gamma rays produce a full erythema dose.

The minimum wave length of radiations should always be known. Spectrometric analysis of the roentgen radiation gives the only absolute control of radiations. We use a Seeman spectrograph. Spectrographic measurements are seen in Figure 2. The minimum wave length of x-rays produced with 211 Kilovolt, 1 mm. copper and 1 mm. aluminum filter and 25 milliamperes is 0.06177 A. U. The effective wave length of the bundle of rays indicated by the shadow extends from 0.06177 to 0.26 and the average wave length of the entire bundle is at 0.12354 Angstrom Units expressed as A. U. Hence the effective wave length is about twice the minimum wave length.

If the peak voltage is known, which may be measured by a sphere gap, then the minimum wave length may be calculated by dividing the Planck constant 12.354, expressed p, with the peak voltage, designated V, i. e. $\frac{p}{V} = \lambda$ or $\frac{12.354}{200{,}000} = 0.06177$ A. U. (One A. U. $= 10^{-8}$ cm. or 0.00000001 cm.) Thus minimum wave lengths for all peak voltages can be calculated as seen in Table I.

TABLE I

THE DETERMINATION OF THE MINIMUM WAVE LENGTH IN A. U. BY THE EQUATION $\frac{P}{V} = \lambda$ IN WHICH P IS 12.354 AND V THE PEAK VOLTAGE

VOLTAGE	MINIMUM WAVE LENGTH IN A. U.	EFFECTIVE WAVE LENGTH CALCULATED AS 2 X
100,000	0.12354	0.24708
200,000	0.06177	0.12354
300,000	0.04178	0.08956
400,000	0.03038	0.06076
500,000	0.02471	0.04942
600,000	0.02089	0.04178
700,000	0.01763	0.03526
800,000	0.01543	0.03086
900,000	0.01372	0.02744
1,000,000	0.01235	0.02470

OUTLINE OF TREATMENT

The patient enters the hospital thirty-six hours before the scheduled time of treatment. A complete blood count including differential count, blood chemistry and Wassermann test, virulency test of cervical and vaginal secretions, hydrogen ion determination of cervical and vaginal secretions, cystoscopy, and proctoscopy are done.

Blood chemistry is important to determine retention of nitrogen. Radiations should be given guardedly and controlled by subsequent nitrogen determinations if

retention is present at the first examination. Radiations cause an increase in the retention of the blood nitrogen. If this is added to a retention already existing a toxemia might ensue proving lethal to the patient.

A hemoglobin percentage of 50 or less, a red cell count of 2,500,000 or less, and a leucopenia contraindicate radiations as the existing anemia will rapidly increase from the large doses of radiations necessary for the treatment of carcinomas. In such instances an arrest of bleeding and discharge should be sought by an application of 50 mg. radium element intracervically for twenty-four to thirty hours. Should the anemia improve due to arrest of hemorrhage and septicity then a complete treatment may be carried out. Transfusions of whole blood may be necessary.

The virulency test is adapted to the technic of Phillip and Ruge. A positive reaction contraindicates all local manipulations. The infection should be combated with antiseptic douches, and roentgen radiation may be given in the meantime until a negative virulency test is obtained, when radium insertions can be safely made.

The hydrogen ion test is made from a purely investigative viewpoint. It has been stated that the P_H turns towards the acid side in the presence of carcinoma and we desire to find out how early this phenomenon may appear.

At this time the outline of the pelvis is taken with the caliper and entered on tracing cloth.

Cystoscopic and proctoscopic examinations are made routinely. Invasion of the rectal or bladder wall is a contraindication to the use of radium. However, roentgen rays may be given.

If all these tests are negative then contraindications to the insertion of radium do not exist. The patient is prepared surgically and is placed under gas anesthesia the next morning. Vaginal and bimanual examinations are again made and recorded. The position, mobility, consistency, shape and depth of the uterus, the direction of the uterine axis and the extent of the carcinoma are determined and entered on the tracing linen. Afterwards the radium equal intensity curves are entered (see Fig. 3). The linen tracing is then placed on the equal intensity curves of the roentgen rays, which are permanently cemented to a drawing board (see Fig. 4). Thereby it is possible to calculate the total radiation dose attained at any point within the pelvis. It should nowhere be higher than 4.5 E. D. throughout the radiation fields and this dose must be scattered in fractions over fifteen to thirty days.

After dilatation of the cervical canal a biopsy specimen is taken and the radium capsule containing 50 mg. element and having a wall thickness equal to 2 mm. brass placed intracervically. Firm packing pushes the bladder and the rectal mucous membranes away as far as possible. A retention catheter is placed in the bladder to keep it empty. The radium insertions are repeated twice at eight day intervals. On the intervening days roentgen ray treatments are given. The duration of treatment depends on the calculations made on the tracing (see Fig. 5). The patient is permitted to be up and about during intervals between the radiation.

The technic of radiation in carcinomas of the uterine body is as follows: The uterine cavity forms a triangle, the apex is at the internal os, the base is formed by the fundal wall. The distance from one tubal uterine os to the opposite tubal uterine os measures from 2.5 to 3 cm. The loss of intensity at a distance of 3 cm. is one-ninth of the dose attained at the radium tube. Since a tandem applicator cannot be fixed in its location within the uterine wall and may lie towards one or the other lateral walls a homogeneous dispersion of rays is problematical when using a tandem applicator. A "Y" shaped radium applicator has been constructed which permits a separation of the upper arms after it is inserted in the uterus. The set screw is marked and indicates the separation of the arms attained (see Figure 6). The equal intensity curves have been drawn in and they show that the intensity attained at the periphery of the uterus is 4 E. D. if 50 mg. of radium element are inserted in each

arm and the stem and applied for fourteen hours at eight day intervals for a total dose of 6300 mg. el. hours. Hence the distribution of the radium intensities with the Y-applicator seems to be very homogeneous and will attack the entire carcinoma with a lethal dose if the carcinoma is limited within the boundaries of the uterus.

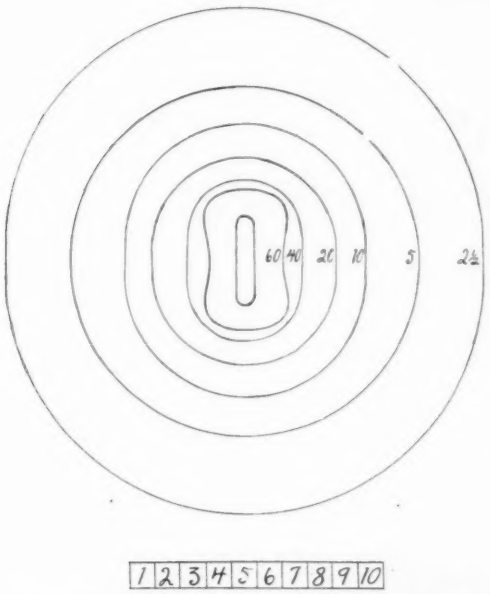

Fig. 3.—Equal intensity curves of 50 mg. el. radium filtered with 2 mm. brass measured in water.

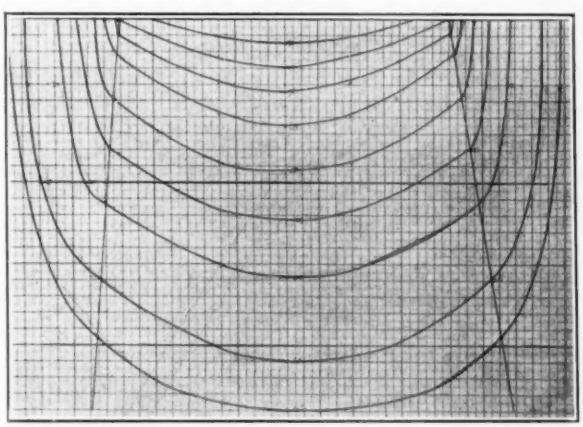

Fig. 4.—Equal intensity curves of x-rays measured in water using the factors: 211 K. V., 0.12354 A. U. effective wave length; 65 cm. focus skin distance; 1.0 mm. copper plus 1.0 mm. brass filter; 15 by 20 cm. size of field; 25 milliampere load.

Invasion of the iliac and inguinal lymph nodes indicates roentgen irradiation. Four fields are used, namely one over each inguinal region and one over each buttocks region. The center of the pelvis is excluded from these radiations so not to cause an overradiation in the uterus, bladder, and rectum.

Radiation sickness is not frequently seen. Radiation cystitis and proctitis occur almost invariably, usually at the time the entire treatment has been concluded. They are self-limited and terminate within two to three weeks. Lithium benzoate in

10 gm. doses well diluted and given every three to four hours relieves the bladder tenesmus. Radiation proctitis is best treated with suppositories of cocoa butter and opium, and a bland diet. In very severe cases fl. extr. coto bark, bismuth subtannate and eventually deodorized tincture of opium in mistura cretae have given better results than any other medication. The skin erythema and epilation are treated with

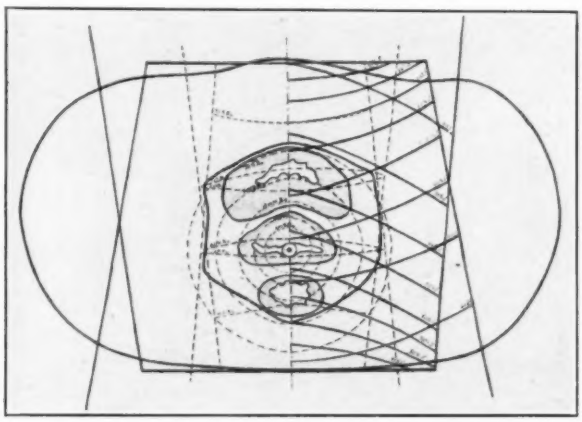

Fig. 5.—Transverse section through female pelvis just above symphysis pubis. Equal intensity curves from radium capsule placed intrauterine are drawn in circles, the radii being taken from Fig. 3. They are designated 50, 100, 200, 400, and 600 respectively which also designates the percentage of erythema doses obtained with a 4800 mg. el. hr. application. They are drawn in interrupted lines. The equal intensity curves of roentgen rays obtained through anterior and posterior fields are drawn in solid lines in one-half of the section. The percentages in relation to the surface intensity are given as 90, 70, 50, etc.

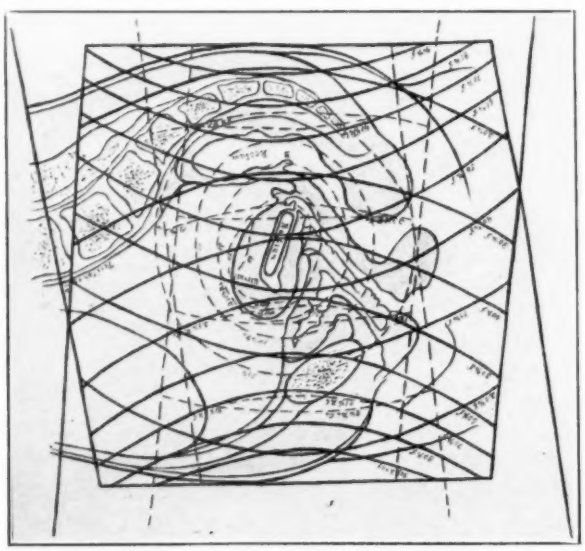

Fig. 6.—Longitudinal section through pelvis with same legends as for Fig. 5.

Dodd's lotion applied on cotton mornings and evenings. Profuse vaginal discharge reacts well to astringent douches.

The diet is a very important means of counteracting the systemic reactions due to radiation. Codliver oil, viosterol, copper and iron, milk, meats, cereals, fats are relied on. Vegetables and fruits are restricted.

Within six to twelve weeks the convalescent period should have ended and the cervix should be healed. If it has not healed we deem it unwise to repeat irradiations and rather prefer to remove the uterus if it can be done. However, should a recurrence occur after a primary healing then the ulceration is treated with interstitial radiation. Platinum needles filled with one, two or three radium cells each of 1 mg. el. strength are inserted at a spacing of 1 cm. from each other. For each estimated cubic centimeter of tissue 120 mg. hours of radium are required. It is best to place the radium needles into the periphery and not into the active growth. Otherwise it is not advisable to repeat a complete course of radiation treatment.

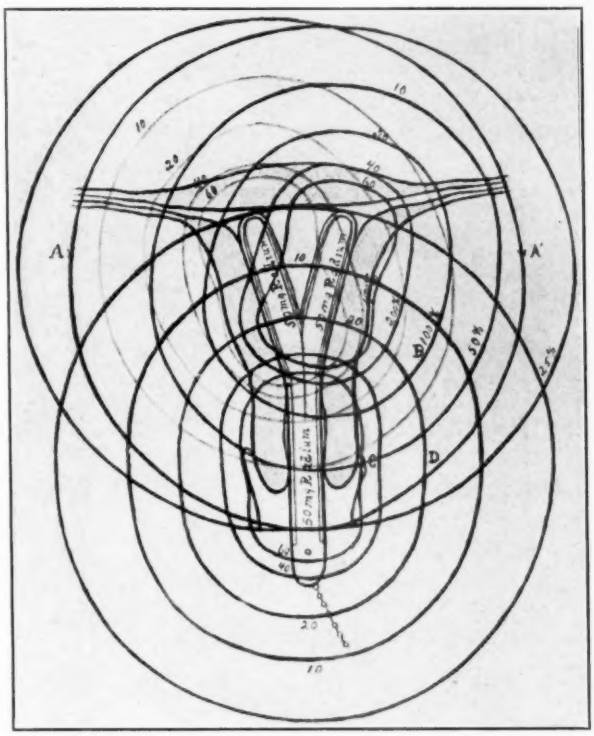

Fig. 7.—Schmitz' Y-shaped radium filter for treatment of carcinoma of the uterine body. It also makes an ideal applicator for the treatment of hemorrhagic metropathies and myomas, as the capsules are held in each uterine fundal angle and thus unintentional cauterization of the internal os is avoided.

Latent complications are stenoses of the cervical canal with pyometra. The patients complain of a mid-pelvic pain, relieved by a sudden discharge of a large amount of purulent fluid. Dilatation of the canal and insertion of a rubber T drain will relieve the complication. Lateral pain in the pelvis usually indicates compression or invasion of ureters with retention hydronephrosis. Ureteral catheterization and pyelography should be used to corroborate the clinical diagnosis. Dilatation of the ureter may cause temporary relief. In some instances in which the carcinoma had healed, resort to transplantation of the ureters was made. Several patients have thus been permanently relieved. Pressure on pelvic nerves is indicated by intense pain and often paralysis of the extremity. Repetition of the roentgen treatment may give the patient relief. Patients unable to walk on entrance to the hospital have reacted so speedily to the scattered fraction method that they left the hospital walking.

It is obvious that changes in the radiation technic were made with an improve-

TABLE II

FACTORS USED IN ROENTGEN TREATMENT FOR EACH PERIOD TO SHOW PROGRESS IN DEVELOPMENT OF TECHNIC

Periods	1914 - 1919	1920 - 1921	1922 - 1923	Since 1924
Transformer	Snook Cross Arm Type		Cross Arm Type to Deliver 300 Kv.	
Type of Tube	Standard Coolidge Treatment with Broad Focus		200 Kv. Air-Cooled Coolidge	250 Kv. Water-Cooled Coolidge
Peak Kilo Voltage	110	140	211	211
Filter: Copper plus Aluminum	6 mm. Al.	0.5 mm. Cu. plus 1.0 mm. Al.	1.0 mm. Cu. plus 1.0 mm. Al.	1.0 mm. Cu. plus 1.0 mm. Al.
Focus Skin Dist.	25 cm.	65 cm.	65 cm.	80 cm.
Size of Fields	25 sq. cm.	225 sq. cm.	225 to 400 sq. cm.	225 to 400 sq. cm.
Number of Fields	8 to 20	2 to 5	2 to 5	2 to 5
Dose to Ea. Fld.	150 mamp. min.	1050 mamp. min.	1000 mamp. min.	1250 mamp. min.
Interval	8 to 20 days One fld. daily	One hr. daily 6 to 15 days	One fld. daily 2 to 5 days	5×250 mamp. min. Every third day to each field
Depth Dose at 10 cm.	About 20%	About 35%	44%	48%
Units in "r"			800 without Backscatter	1200 without Backscatter

ment in apparatus. Table II shows the periods and the factors for each one of the periods. In the near future a 1,000,000 kilovolt transformer and a cascade tube able to carry a load of 900 to 1000 kilovolts will be installed. The statistics presented in Table III demonstrate that the five year good end-results improved with each improvement in the roentgen technic as the radium dose has always remained the same. One may anticipate an improvement in good end-results with the use of such ultra short wave length roentgen rays, as the biologic reaction increases in direct proportion to the decrease in the wave length of the rays.

SUMMARY

1. The physical principles of the production of x-rays and radium should be known to obtain the best results in the treatment of malignant diseases by irradiations.

2. The methods of application, the scattered fraction method of treatment, the factors which describe the quality of the rays, the definitions of the erythema dose and the international roentgen unit, termed r, have been discussed.

3. The dose is the product of the radiation intensity and the time and

TABLE III

	PERIOD: 1914 - 1919					1920 AND 1921				
Clinical Group	1	2	3	4	Total	1	2	3	4	Total
Total number admitted	5	16	76	35	132	9	13	26	29	77
Total 5 year good end-results	5	7	7	0	19	6	6	2	0	14
Per cent 5 year good end-results	100.0	43.75	9.21	0	14.39	66.67	46.75	7.69	0	18.38

	PERIOD: 1922 AND 1923					1924 - 1927				
Clinical Group	1	2	3	4	Total	1	2	3	4	Total
Total number admitted	9	19	59	36	123	12	14	61	69	156
Total 5 year good end-results	7	7	11	0	25	10	6	16	3	35
Per cent 5 year good end-results	77.78	36.84	18.65	0	20.32	83	42.85	26.23	4.35	22.43

GRAND TOTAL 1914 - 1927					
Clinical Group	1	2	3	4	Total
Total number admitted	35	62	222	169	488
Total 5 year good end-results	28	26	36	3	93
Per cent 5 year good end-results	80.0	41.94	16.36	1.72	19.14

has been given in E. D. and r. The effective wave length measured with the spectrograph gives the only absolute control of the quality of rays.

4. The use of equal intensity curves of radium and x-rays on the transverse diagram of the patient's pelvis has been demonstrated. Thereby it is possible to apply an intense radiation dose of 4 to 5 E. D. throughout the pelvis, this dose being considered lethal to the majority of uterine carcinomas. Irreparable injuries to the pelvic organs by the rays can only be avoided by the use of the equal intensity curves and the diagram.

5. The preparation of the patient, the contraindications to radiation therapy, and the treatment of local and systemic complications have been considered.

25 EAST WASHINGTON STREET.

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AN ANALYSIS OF THE MENSTRUAL CHANGES IN TUBERCULOUS WOMEN*

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STUDENTS of tuberculosis are constantly being reminded of the profound alterations in the physiology of unrelated organs and systems which are brought about by the presence of an active tuberculous process in the lungs, intestines, or elsewhere. Pulmonary tuberculosis especially can no longer be regarded as a disease of the lungs alone but rather as a systemic condition whose presence is reflected in every tissue of the body.

The pathologic physiology of the gastrointestinal tract, the blood, the nervous and circulatory systems in patients suffering from tuberculosis has been well worked out and numerous studies have been made on the blood pressure variations and basal metabolic rates, but in no system, perhaps, are the changes so manifest as those found in the physiology of the female genital tract. Other investigations of these changes have been made, notably by Norris and Macht, but none, so far as we have been able to determine, from the same angle as that which follows.

This report is based upon an analysis of 200 detailed menstrual histories obtained consecutively from women at the sanatoria in and around Saranac Lake. All of these patients have active pulmonary tuberculosis; 22 have intestinal, 3 laryngeal, and one cervical gland lesions in addition. The ages vary from sixteen to forty-eight, with the largest group falling in the third decade of life. With the exception of minor treatment for leucorrhea and a few instances of curettage, none of the patients in this series had had operations on the genitalia.

While it is appreciated that this series is small and that there are far too few cases in the various groups when the subdivisions have been made to warrant any definite conclusions, this report would seem to be of interest for the purpose of demonstrating trends rather than that of actual figures or percentages.

An analysis of the age groups shows 13 in the sixteen to twenty group; 125 between twenty and thirty; 47 between thirty and forty, and 15 over forty years of age. The group over forty is small because of the confusion which may arise with symptoms of the menopause. On the basis of extent of disease according to the National Tuberculosis Association classification, there were 34 minimal, 114 moderately advanced, and 52 far advanced cases.

The age of puberty was thirteen and four-tenths years for the minimal cases; twelve and eight-tenths years for the moderately advanced, and thirteen and nine-tenths years for the far advanced patients. This is

*Read, by invitation, at a meeting of the New York Obstetrical Society, March 8, 1932.

unexplained as the average age for the various groups is practically identical (twenty-seven and five-tenths years).

In answer to the question, "Have you noticed any change in your menses since beginning the cure?" 55.8 per cent of the minimals, 58 per cent of the moderately advanced, and 67.3 per cent of the far advanced cases answered in the affirmative. All of these changes were not for the worse as an appreciable number reported a return to a twenty-eight-day interval or improved flow, since entering the sanatorium. When calculated on the basis of age groups, 55 per cent of the girls under thirty showed changes since the onset of tuberculosis and 68 per cent of the patients over thirty. This latter increase is not due to the approaching menopause as the percentage is the same for the fourth and fifth decade groups separately.

Previous to the onset of tuberculosis 20 per cent of the entire series gave a history of irregularity; since the diagnosis of tuberculosis has been made 26 per cent have been irregular. The extent of the disease seems to have but little influence on the incidence of irregularity as shown in Table I.

Sixteen and one-half per cent of the series have had longer inter-

TABLE I. IRREGULARITY

	BEFORE TUBERCULOSIS	SINCE TUBERCULOSIS
Minimal	20.6%	29.4%
Moderately Advanced	17.5%	23.6%
Far Advanced	25 %	29 %
Total	20 %	26 %

menstrual periods since the onset of tuberculosis while 18 per cent report shorter intervals and 66.9 per cent no change. As shown in Table II, the minimal cases show the greatest incidence of change and the incidence of longer or shorter intervals is very similar for all groups.

The average number of days of flow for all groups is four and nine-tenths before the onset of tuberculosis; four and six-tenths days since. The minimal cases decreased on the average from five to four and six-tenths days; the moderately advanced from five and one-tenth to five; and the far advanced from four and eight-tenths to four and three-tenths days. We are unable to explain the discrepancy in the moderately advanced group.

A history of flow lasting more than six days, exclusive of puberty or miscarriages, was given by 20.5 per cent of the minimal, 18.4 per cent of the moderately advanced, and 11.5 per cent of the far advanced cases. This makes an average figure of 16.8 per cent for the entire series and suggests that hypermenorrhea becomes less common as the disease progresses.

Taking a history of one or more periods skipped (exclusive of the

first years after puberty, pregnancy, and operated cases) as a criterion, 13 per cent of the minimal cases, 27 per cent of the moderately advanced, and 26 per cent of the far advanced cases had had periods of amenorrhea. These figures are strikingly high when compared with those of Norris. It is our impression that the onset of the disease or an increase

TABLE II. LENGTH OF INTERMENSTRUAL PERIOD

	LONGER	SHORTER	NO CHANGE
Minimal	23.5%	20.6%	66 %
Moderately Advanced	15 %	17 %	68 %
Far Advanced	15.6%	17.6%	66.8%
Total	16.5%	18 %	66.9%

in the lesion is the commonest time for the appearance of amenorrhea and that, while the incidence in the moderately advanced and far ad-

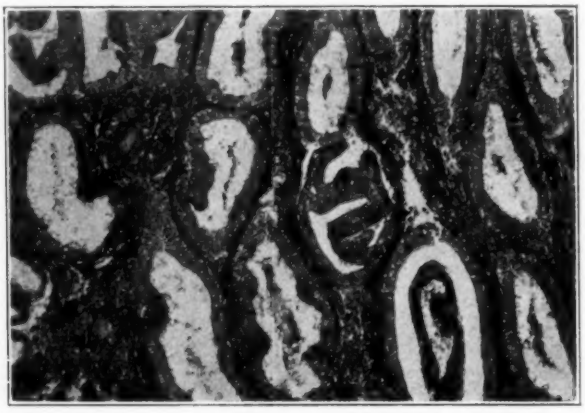

Fig. 1.

vanced groups is the same, when once established it tends to last longer in the far advanced cases. That age is also a factor is evident when we see that the incidence in patients below thirty is 18.8 per cent while for those over thirty it is 32 per cent in each decade.

Of similar interest was the history of intermenstrual bleeding, exclusive of miscarriages, since the onset of tuberculosis. In the minimal group, there were 4 cases; in the moderately advanced 7, and in the far advanced group 3 patients with a history of metrorrhagia since coming to the sanatorium. The incidence for the entire series is 7 per cent with a frequency twice as great in the minimal cases as in the other two groups.

We have had occasion to curette a number of these cases of metrorrhagia in tuberculous women with the hope of making a diagnosis of the cause. The findings have been very confusing as the microscopic picture varies from that of an apparently normal resting endometrium through that of the different cyclic changes. A few cases of undoubted endome-

trial hyperplasia have been encountered but in a large proportion of cases the pathologist was unable to solve the question of why bleeding occurred (Figs. 1 and 2).

The differences in the amount of flow for each group since the onset of tuberculosis is shown in Table III. It will be seen that there is a greater tendency to no change or a decrease than towards more flow in all the groups.

Dysmenorrhea would seem to be a common complaint, although Tobler and Schaffer find that 70 to 75 per cent of otherwise normal women suffer more or less at the time of flow. This series shows a slight increase in the total number of cases of dysmenorrhea in each group since the onset of tuberculosis, but a significant rise in the number of severe cases. Table IV shows the type of dysmenorrhea. The percentages are figured on the total number of cases of dysmenorrhea in each class of

Fig. 2.

tuberculous lesion rather than upon the entire group. Calculated on the basis of the entire series, 68 per cent of the tuberculous women had dysmenorrhea divided as follows: 18.3 per cent congestive type, 53 per cent obstructive, 28.6 per cent mixed, and one case of postflow pain in a

TABLE III. AMOUNT OF FLOW

	UNCHANGED	MORE	LESS
Minimal	67.7%	14.7%	17.6%
Moderately Advanced	81.7%	6.1%	12.2%
Far Advanced	69 %	5.7%	25 %

TABLE IV. TYPE OF DYSMENORRHEA

EXTENT OF DISEASE	PREMENSTRUAL	MENSTRUAL	MIXED
Minimal	29.0%	50 %	28 %
Moderately Advanced	16.0%	55.5%	28.4%
Far Advanced	16.0%	48.4%	35.5%
Total	18.3%	53.0%	28.6%

single girl whose menses lasted three to four days and whose pain appeared on the fifth day. As only nine girls in the entire series weighed less than one hundred pounds (five of whom had no dysmenorrhea and the remainder no more or no less than they had before the onset of tuberculosis), the theory of malnutrition as a cause of menstrual pain in tuberculous women does not seem tenable.

Additional data on the question of dysmenorrhea is given in Table V where the pain is classified as mild, moderate, or severe. This is an arbitrary grouping and depends upon the patient's own reaction to her pain. The table also shows that about 10 per cent of the girls have less pain than they had before and a somewhat larger number more.

Symptoms other than pain noted by these women are shown in Table VI. While no figures are at hand to support the contention, we believe that an equal number of so-called normal women would show about the same results with the exception of the large number who complained of prostration and premenstrual, menstrual and postmenstrual elevations of temperature. In this study premenstrual and menstrual fever was taken to be 99° F. or over, while in a previous analysis, somewhat more accurate criteria were followed and a lower incidence discovered. It is our impression that the menstrual elevations of tempera-

TABLE V. DYSMENORRHEA

	MINIMAL	MODERATELY ADVANCED	FAR ADVANCED
None	32.3%	32.4%	44.2%
Mild	8.8%	24.5%	17.3%
Moderate	32.3%	24.5%	17.3%
Severe	26.4%	18.4%	21.1%
Less Since Onset	11.7%	10.5%	10.0%
More Since Onset	17.6%	12.2%	12.0%

TABLE VI. NUMBER OF CASES SHOWING SYMPTOMS OTHER THAN PAIN

SYMPTOM	MINIMAL	MODERATELY ADVANCED	FAR ADVANCED	TOTAL
Distention	0	0	1	1
Diarrhea	0	2	0	2
Sore Breasts	0	4	0	4
Nausea	1	3	2	6
Headache	6	19	4	29
Fatigue	3	6	1	10
Vomiting	0	3	1	4
Weakness	0	2	0	2
Irritable	2	2	1	5
Syncope	0	0	1	1
Epistaxis	0	0	1	1
Nervousness	2	2	3	7
Vertigo	1	0	0	1
Hysterical	0	0	1	1
Prostration	5	29	17	51
Premenstrual* Fever	58.8%	55.2%	59.6%	57.0%
Menstrual Fever	14.7%	7.8%	7.6%	9.0%
Postmenstrual Fever	5.9%	4.8%	3.8%	4.5%

*Premenstrual, menstrual, and postmenstrual fever is 99° F. or over.

ture occur in patients who are not doing well. The postmenstrual fever shown by the minimal cases was a continuation of the premenstrual and menstrual elevations; the same condition holds in the moderately advanced and in addition half the cases were progressing. In the far advanced group both cases had intestinal tuberculosis and one, in addition, who had a tuberculous larynx had chills and a temperature of 102 to 104° F. on the first day after the menstrual period.

The question of leucorrhea was studied in single women only and an incidence of 41 per cent for the entire group noted. It was contrary to our expectations to find the highest incidence among the minimal cases and the lowest among the far advanced. The details are shown in Table VII.

It is interesting to note that there is less leucorrhea among the tuberculous women who are popularly supposed to be "run down" than occurred before they became ill. An intermittent leucorrhea is the more frequent type in all the groups, but there are proportionately more cases of a constant discharge in the minimal cases than in those that are advanced. Similarly all the positive cases in the far advanced group had a scant discharge only, while 18 per cent of the minimals described it as profuse.

We were unable to show any definite relation between pregnancy and onset of tuberculosis in this series. Sixty married women have been included, of whom 34 have been pregnant. Twenty-seven went to term one or more times. Two patients dated the onset of their tuberculosis to

TABLE VII. LEUCORRHEA (SINGLE WOMEN ONLY)

TYPE	MINIMAL	MODERATELY ADVANCED	FAR ADVANCED	BEFORE TUBERCULOSIS	SINCE TUBERCULOSIS
Incidence	44.0%	38.2%	41.0%	46.0%	41.0%
Intermittent	72.7%	80.0%	85.0%	88.0%	79.2%
At Menses Only	18.0%	62.5%	33.0%	38.6%	37.8%
Constant	27.2%	20.0%	15.0%	12.0%	20.7%
Slight	81.0%	90.0%	100.0%	96.0%	90.0%
Profuse	18.0%	10.0%	0	4.0%	10.0%

abortions, and one moderately advanced case had a therapeutic abortion done after the diagnosis was made. One far advanced case, who has had tuberculosis for fifteen years, has had two babies, the last three years ago, and one miscarriage seven years ago. One moderately advanced patient, para ii, dated the onset of her tuberculosis to the time of her last confinement but the evidence is not conclusive and another moderately advanced case had a confinement six months before her tuberculosis was diagnosed. The remainder showed no relation whatsoever.

Intestinal tuberculosis was present in 22 patients, but this complication seems to have no influence on the incidence of changes in their menses since beginning the antituberculous régime as compared with the entire group.

Of the 80 girls who gave a history of hemoptysis, an incidence of 40 per cent for the series, 26 per cent reported the occurrence of pulmonary hemorrhages only at the time the menses were present; 53.7 per cent between periods; 10 per cent showed no relation, and 10 per cent could not recall whether or not they were menstruating at the time. Thus, while hemoptysis did occur in 26 per cent of the cases at the time of catamenia, a cause and effect relation is not clear except in the occasional case. One minimal case, a section of whose endometrium is shown in Fig. 1, "streaked" daily over a period of three and a half months, while we were endeavoring to stop her metrorrhagia with small doses of x-ray. Radium was finally used and when the uterine bleeding was stopped the pulmonary hemorrhages also ceased and have not recurred.

The number of patients in this series who were taking pneumothorax is too small to warrant a detailed analysis but the findings have been of sufficient interest to stimulate the further study which is now in progress. Suffice it that in a large percentage of cases the effects of collapse therapy appear to have a deleterious influence on the menstruation and only a few show the improvement noted by Caussimon.

CONCLUSIONS

No attempt can be made to draw up a list of definite conclusions from such a series as is presented in this report, but the necessity of revising many of our former ideas of the influence of tuberculosis on the menses is apparent. Particularly is this true of the questions of amenorrhea and the influence of collapse therapy on the menses. Whether or not menstruation, with the coincident lowering of capillary permeability, predisposes to hemoptysis is a fruitful field for further study and holds many possibilities. Certainly it is true however that tuberculosis exerts a profound effect through some as yet undetermined mechanism upon the menstrual cycle and that we are only beginning to appreciate its true extent.

The author wishes to express his thanks to Drs. Helen Evarts and John Booth, without whose assistance this report would not have been possible.

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DISCUSSION

DR. M. D. MAYER.—It seems to me that in the fairly advanced cases, especially in the third decade of life, it would be rational to advise routine radiation of the ovaries in order to give at least a one- or two-year complete amenorrhea. It is almost impossible in the first half at least of the third decade and at least unlikely in the second half of the third decade, to produce a permanent amenorrhea with the pieceable doses of x-ray. In a fairly large series of therapeutic

abortions for tuberculosis, produced by means of x-ray, it has been found that the large majority of cases do very well clinically as far as their tuberculosis is concerned after the incidental long-term amenorrhea which occurs after the abortion has taken place.

DR. HARVEY B. MATTHEWS.—I believe it can be safely said that our conception of menstruation, pregnancy, and labor in relation to tuberculosis, will have to be more or less revamped.

It may be in order to suggest that these menstrual disturbances could be brought about by at least three different pathologic conditions, First, the tuberculosis itself; the constitutional change brought about by the tuberculosis in any of its forms, but more particularly the pulmonary type, may have something to do with these changes, because these girls do improve during an amenorrhea; second, the endocrine disturbances that we know go with tuberculosis, particularly pulmonary tuberculosis, may have, and undoubtedly do have considerable influence on these changes; and third, changes in the blood chemistry may have something to do with these, since we know that the calcium content of the blood in tuberculosis is lowered, as it is during the menstrual and postmenstrual periods. So if the calcium coefficient is lowered in general tuberculosis, a constitutional disease, then it is lowered further during the time of the menstrual flux. It would naturally, therefore, be supposed that there would be an exacerbation of the tuberculous process during the menstrual period. That is shown by the rise in temperature in 42 per cent. I believed this percentage was much higher.

Formerly at Saranac Lake there was a good deal of opposition to the idea of an irradiation amenorrhea. There were quite a few patients who were suffering from hemorrhages of various kinds and who also had severe dysmenorrhea. I suggested producing amenorrhea with radium, but the idea was not received favorably. However, several patients were irradiated and in every instance there was improvement in the tuberculosis. I would recommend a temporary amenorrhea in suitable cases. The "dosage" of radium can now be fairly definitely controlled, and I can see no harm in its use and I have seen much benefit accrue to the tuberculosis. We have accumulated enough data to be fairly certain that preconception irradiation is a perfectly safe procedure as regards future pregnancy.

DR. JAMESON (closing).—We got the idea of inducing amenorrhea in pulmonary tuberculosis from German authorities, but the local ultra-conservative group would not let us do it. I have had about six cases and all of them were improved. I talked to some of the girls, particularly at Stony Wold, and they said they would be glad to have their menstruation cut out because they all felt very much worse at the time of their periods; and I believe I am correct in insisting that the lung findings are always more marked at the time of menstruation than at any other time.

As regards calcium metabolism, the work done at Stony Wold on the nondiffusible-diffusible ratio in the blood and spinal fluid, was found of no value in determining activity or prognosis.

I am firmly convinced that these girls, who have a fever during the menstrual period, should have an amenorrhea established: it does not matter whether it is permanent or not in that case. Some men think the temperature during menstruation indicates a blood stream infection with tubercle bacilli, and the Germans and French claim that they have obtained tubercle bacilli from the blood stream. Several attempts have been made at Trudeau, but were unsuccessful in finding the tubercle bacillus in the blood stream.

EPITHELIAL REGENERATION IN THE UTERINE GLANDS AND ON THE SURFACE OF THE UTERUS*

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ONE of the characteristics of the uterine epithelium is its periodic destruction and regeneration. The periodic loss of the epithelium occurs during menstruation in the human being and in the primates and during estrus in the lower mammals. This reaction shows great variations in the various types of mammals and in different individuals. In women, according to some investigators, only a small part of the epithelium and of the underlying stroma is cast off. According to others, the whole epithelium and a large part of the tunica propria, at least the whole of the compacta and most of the spongiosa, are eliminated. The last view can hardly be considered applicable to the average normal type.

The regeneration of the uterine epithelium occurs with surprising rapidity. In guinea pigs, a complete replacement of the epithelium is found within a few hours after its desquamation. In women, the regenerative processes begin as early as the third day of menstruation[1] and develop very rapidly. Another surprising fact is the almost complete absence of mitotic figures during this early regenerative stage. The actual proliferative phase, during which a large number of mitoses can be seen, occurs later, when the new epithelium is almost completely formed. These two facts, i. e., the rapidity of the new epithelization and the lack of mitotic figures, cannot be well explained by the generally accepted theory, that the uterine epithelium regenerates from the epithelium of the deep glands which has escaped destruction, or from remnants of the old epithelium.

In 1890, Duval,[2] and later Johnstone,[3] and Heape,[4] expressed the view that at least a part of the uterine epithelium regenerates in a different way, by the actual differentiation of the superficial cells of the tunica propria. Duval pointed out that, since the uterine epithelium, as well as the tunica propria, were both of mesodermic origin, it was not inconceivable that such epithelium could be formed by a transformation of mesodermic cells.

More than ten years ago, in studying the uteri of guinea pigs, killed at different times after copulation, I noticed that, in several specimens, the new uterine epithelium looked as if it were suddenly arising through a differentiation of the most superficial cell layers of the tunica propria. Being out of accord with such an interpretation on theoretical grounds

*Read, by invitation, at a meeting of the New York Obstetrical Society, March 8, 1932.

and realizing that the evidence offered by this material was insufficient, I did not continue the observations. Recently, however, in studying the epithelium of uterine glands, I have been impressed by the fact that the epithelium in these glands is desquamated to the very tip of the gland and then a process of regeneration of an entirely new glandular epithelium quickly ensues. The changes within the glands did not appear

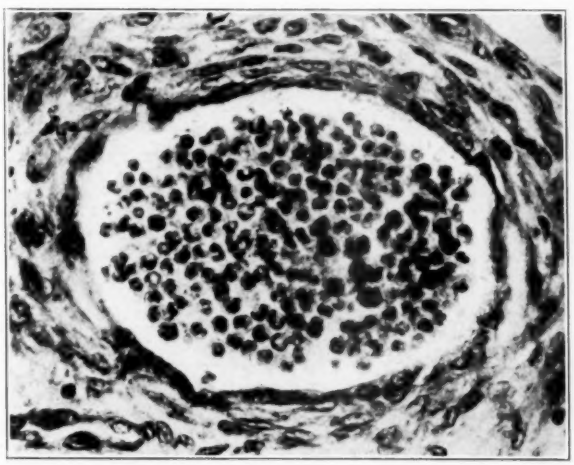

Fig. 1.

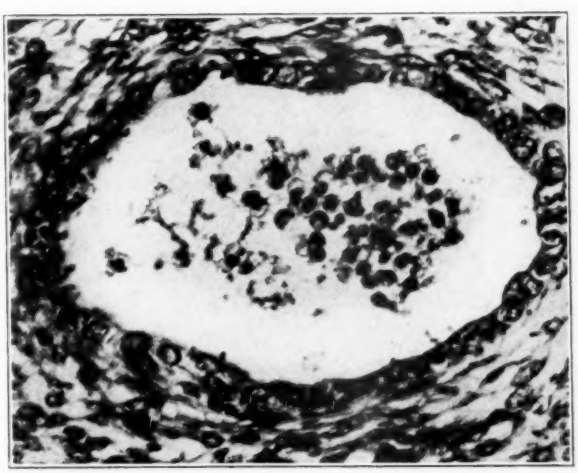

Fig. 2.

to be synchronous with the changes on the surface of the uterus, and this may have been the reason why they escaped the attention of previous investigators.

The desquamative and regenerative processes in the glands are much simpler and they clearly indicate that the new epithelium is formed by the actual differentiation of the superficial cells of the tunica propria.

One may recognize a series of stages succeeding one another in a typical fashion. First, there is a stage of desquamation, during which the epithelium disintegrates and falls into the lumen of the gland, which is soon filled with a large number of desquamated cells and leucocytes (Fig. 1).

The next stage is characterized by the gradual differentiation of the superficial cells of the tunica propria. These cells are small and have a round or slightly elongated, oval, or elliptic nucleus and a very small amount of cytoplasm (Fig. 1). They resemble undifferentiated embryonic cells and are very abundant within the tunica propria. Their nature has been the subject of a great deal of controversy. We adhere to Minot's view considering them to be embryonic in character. These cells become rounded and gradually form a continuous lining on the surface of the naked gland (Fig. 2).

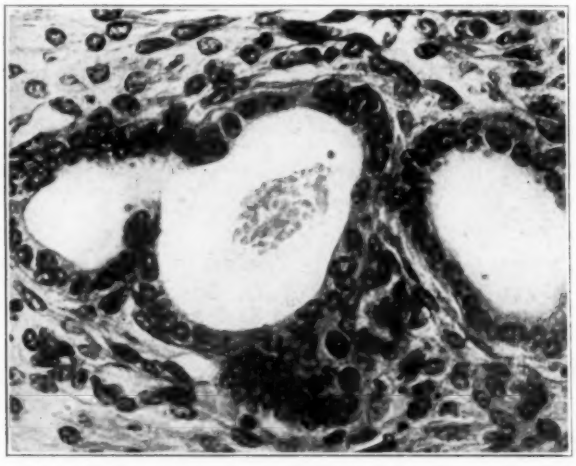

Fig. 3.

A period of growth now follows during which these cells, as well as their nuclei, become larger and display a progressive differentiation from a round to a cuboidal form (Fig. 3). In continuation of this, an extensive proliferation is initiated during which a large number of mitoses can be seen (Fig. 4). The mitoses appear, en masse, when the new epithelium is totally differentiated and are more numerous near the surface. They evidently represent an active proliferation of the newly formed epithelium.

Similar changes and a corresponding succession of stages occur at the surface of the uterus. In typical cases the whole of the uterine epithelium is cast off (Fig. 5). Below this, a basement membrane is often seen connected with cells resembling fibroblasts. Such a membrane appears also in the glands and is usually cast off with the epithelium. The superficial undifferentiated cells of the uterine wall are now grouped

together in a heavy, compact zone which reminds one of the compacta, as it has been described in the human being during premenstruum and menstruation (Fig. 5). Hitschmann and Adler[5] and others, who described this zone, considered it as a differentiation of a false decidua. In the light of the present investigation, it seems to represent a heavy accumulation of undifferentiated cells near the surface of the uterus as a preparation for the formation of the new epithelial lining.

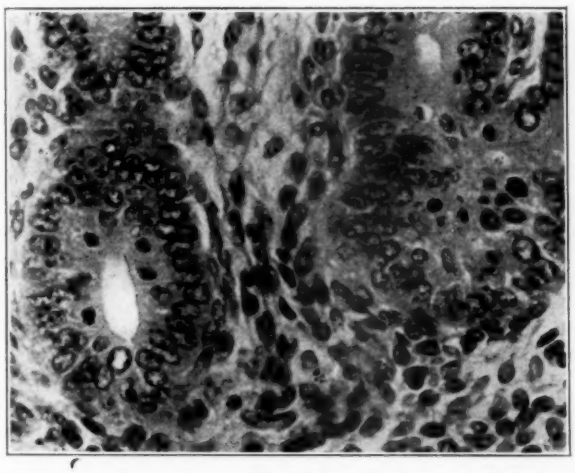

Fig. 4.

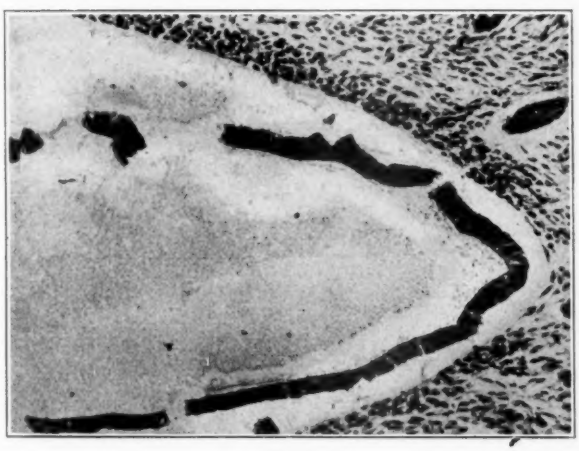

Fig. 5.

Soon after this the growth phenomena are initiated. The most superficial cells become rounded, larger in size, and form a continuous epithelial layer (Figs. 6 and 7). This new epithelium is gradually separated from the underlying undifferentiated tissue and takes on a cuboidal form. The proliferative phenomena appear after the new epithelium is already formed (Fig. 8). The mitotic figures are numerous and usually located near the surface of the epithelium, as in the glands. It is thus

evident that the restoration of the epithelium occurs before the appearance of typical proliferative phenomena.

The existence of cyclic changes in the epithelium of the uterine glands is of particular interest, because it provides new material for the study of the uterine epithelial regeneration. The changes occurring on the surface of the uterus are very complex and atypical due to several disturbing factors. One of these is the extreme abundance of glandular

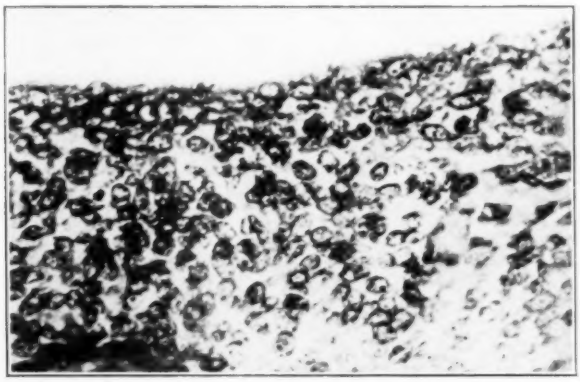

Fig. 6.

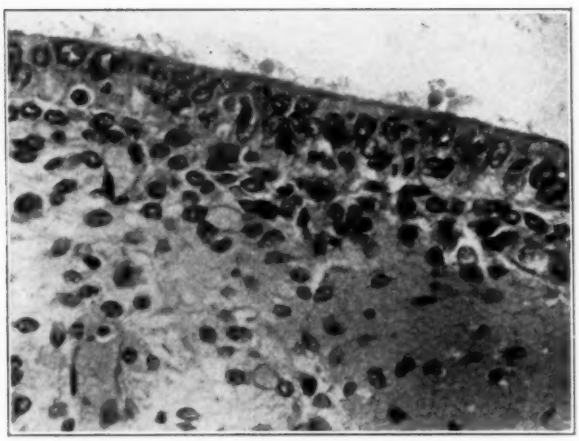

Fig. 7.

ducts ending very close one to another on the surface of the uterus. When the new epithelium is formed, it is almost impossible to decide whether the regeneration began on the surface of the uterus, within the glands or simultaneously in both. It is often possible to interpret the same figure in three different ways, without definite proof of the correctness of any. This disturbing factor does not exist in the deep glands. When the epithelium is desquamated from an entire gland, there is practically no trace of old epithelium left to account for the sudden reappearance of a new epithelial lining.

Another confusing factor is the often extensive destruction of large pieces of tunica propria on the surface of the uterus along with its epithelium. This creates an irregular healing surface, greatly complicating the simplicity of the new epithelial differentiation. In the glands it is only the epithelium and the basement membrane that are cast off, the tunica propria remaining almost intact.

Groups of glands undergoing epithelial replacement are easily recognized by the large number of leucocytes and cellular detriment, filling their lumen. Confusion with glands undergoing cystic degeneration is practically impossible, because of the characteristic structure of their epithelium.

These studies favor the view that the tunica propria of the uterus contains a large number of undifferentiated cells of mesodermic origin,

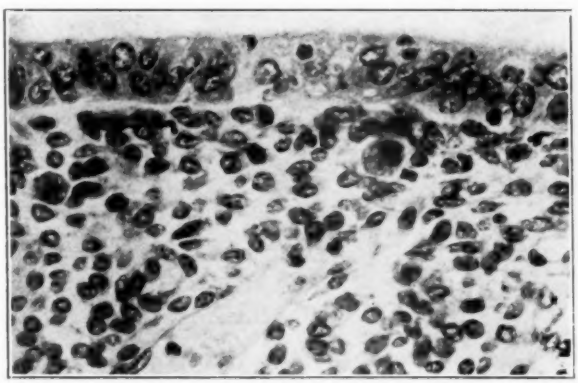

Fig. 8.

which, under favorable conditions, may form epithelial tissue. This occurs on the surface of the uterus, soon after the old epithelium is cast off and also within the deep uterine glands. The new epithelium is completely formed within a very short time. Growth and proliferative phenomena appear later. The replacement of the epithelium within the uterine glands is a much simpler process than the replacement of the epithelium on the surface of the uterus and offers excellent material for an accurate study of this problem.

NOTE: This work has been aided by the Committee for Research on Sex Problems of the National Research Council.

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DISCUSSION

DR. J. A. CORSCADEN.—Is it fair to say that the connective tissue elements of the endometrium can become epithelial because they are of the same mesoblastic origin?

DR. G. N. PAPANICOLAOU.—The uterine epithelium is evidently formed by undifferentiated, embryonic cells present within the tunica propria and not by differentiated connective tissue elements. The fact that the epithelium as well as the tunica propria of the uterus are both of mesodermic origin permits us to approve of such an interpretation from an embryologic point of view.

DR. W. H. CARY.—I would like to know what relationship this might bear practically and clinically to the traumatism of too deep curettement; whether destruction brought about by curetting could interfere with the regeneration of the uterine epithelium.

DR. G. N. PAPANICOLAOU.—We suppose that the regeneration of the uterine epithelium after curettage occurs in the same way as normally, i. e., by a differentiation of embryonic tunica propria cells. We do not believe that destruction brought about by a mild curetting would interfere with the regeneration of the uterine epithelium, since numerous regenerative cells are scattered through the whole of the uterine mucosa. Of course a very deep curettement might cause a certain damage by destroying too much of the regenerative reserve cell material.

DR. W. H. CARY.—I am referring to curettage for hemorrhage in cases of incomplete abortion, whether damage could be done where it is carried down to the muscle, if the destruction could be such as to interfere with regeneration of the uterine epithelium.

DR. G. N. PAPANICOLAOU.—Our discussion on the regeneration of the uterine epithelium after curettage is purely theoretical, as we have not undertaken experimental work along this line. From a theoretical standpoint we would be inclined to believe that a very severe curettement carried down to the muscularis would cause permanent injury to the uterine epithelial wall and to its regenerative ability.

DR. MAYER.—Am I right in assuming that Dr. Papanicolaou has found exactly the same pictures in human uteri as in guinea pigs?

DR. G. N. PAPANICOLAOU.—No. We have not had the opportunity to extend these observations to human uteri. The regenerative changes within the uterine glands have been found by us only recently in guinea pigs. Whether similar changes occur in the human we cannot definitely state. We find a suggestion of such changes in some of the photographs published by other investigators in the human being.

The fact that the uterine glands during the very early stages of the epithelial replacement are filled with dead desquamated cells and phagocytes helps greatly in their identification even with a low power.

DR. G. L. MOENCH.—I would like to ask Dr. Papanicolaou if he has seen any similar epithelial changes in the peritoneum. This membrane, lining the celom formed by the splitting of the mesoderm into the splanchnopleure and somatopleure, is of pure mesodermal origin, yet in the woman at times typical endometrial glands seem to originate from it. Some of us consider the peritoneum to be the source of many adenomyositic processes.

DR. G. N. PAPANICOLAOU.—I recall only one case in which uterine glands were present within the myometrium in a guinea pig. The uterus was highly cystic and the uterine wall greatly distended. The uterine mucosa was very thin. One could gather the impression that this invasion of mucosal elements within the muscularis was an abnormal condition caused by the action of degenerative factors. Otherwise, I have not observed uterine gland inclusions within the myometrium in normal animals. It is difficult to offer any general interpretation for these peculiar morphologic discrepancies.

DR. G. L. MOENCH.—What do you consider the stroma itself, outside of the mesoderm?

DR. G. N. PAPANICOLAOU.—In the light of these investigations the tunica propria of the uterus seems to consist of two distinct groups of cells: some differentiated connective tissue elements and some undifferentiated embryonic cells. The presence of the last group gives a peculiar structure to the uterine mucosa and secures a rich supply of regenerative reserve material. For an organ undergoing repeated and extensive epithelial destructions, as the uterus does, this seems to represent a very well adapted morphologic structure. The same reserve material may be used for another useful purpose, i. e., the differentiation into decidual tissue.

THE BEHAVIOR OF THE EPITHELIUM IN EXPLANTS OF HUMAN ENDOMETRIUM*

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EXPLANTS of human endometrium have been cultured for various purposes. In experiments concerned mainly with the growth in vitro of human malignant tumor tissues, they have been cultured incidentally; in other experiments, they have been explanted with the purpose of testing Sampson's theory of displaced endometrial tissue growth; and finally in studies chiefly of an academic nature, endometrial tissues have been cultured to see what cellular structures, if any, grow.

Cron and Gey[1] cultured endometrium recovered on the second day of menstruation in a plasma medium containing heterologous embryonic extract. After several hours' incubation, they noted an activity of the cells and, for several days, a growth of leucocytes far into the medium. The fixed tissue cells began to emigrate on the second day, when radial outgrowths of spindle cells and sheets of epithelium appeared at the periphery of the tissue fragments. The explants were transferred every four or five days for a month. Although these explants had vital properties, they were discarded because the tissue masses did not increase in size. Cron and Gey concluded that they had demonstrated viability of endometrial tissues removed by curette. Their cultures were not sectioned serially. Heim[2] cultured endometrium in a mixture of female human and chicken plasmas and chick embryo extracts. He reported the growth of a variety of cells, but his statements regarding the nature of the tissue cells growing about his explants are vague. Fragments of endometrium obtained by curette were cultured by Caffier[3] on homologous and heterologous plasma containing embryonic tissue extracts or other fluids. None of these mediums consistently promoted growth: Caffier preserved the vitality of his explants only fourteen days. His explants were stained in toto. He described membranes of cells around the explants, but the character of the cells participating in this growth was not mentioned. Traut,[4] with a fibrinogen solution and diluted embryonic extract containing a trace of sodium linolate, maintained the growth of human endometrial explants about twenty days. His cultures were fixed, stained, and mounted in toto. The growth of new tissue, he stated, was entirely of the stroma or connective tissue portions of the explant; the epithelium, having a long latent period, was overgrown by the stroma cells. Conclusions based only on the microscopic examinations of living explants or even preparations stained in toto are hazardous. None of the authors

*This research was aided by a grant from the Watson K. Blair Fund.

reported the study of explanted endometrium in serial sections, a method now considered necessary.

Accordingly to generally accepted histologic descriptions[5] the lamina propria of the endometrium is a network of reticular fibers condensed into a basement membrane under the epithelium of the surface and glands. This fibrous reticulum is intimately connected with many small polyhedral cells having small processes that anastomose throughout the tissues and adhere to the fibers of the reticulum. The small spaces between the cells contain wandering cells such as lymphocytes or granu-

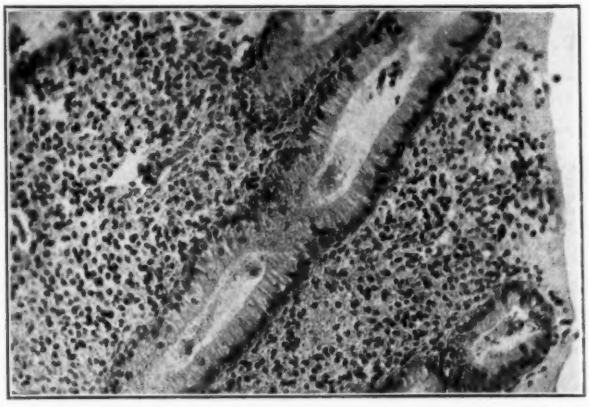

Fig. 1.—An explant four days old with focal regions of necrotic stroma. There is only a slight hyperplasia of the glandular structures. ×270.

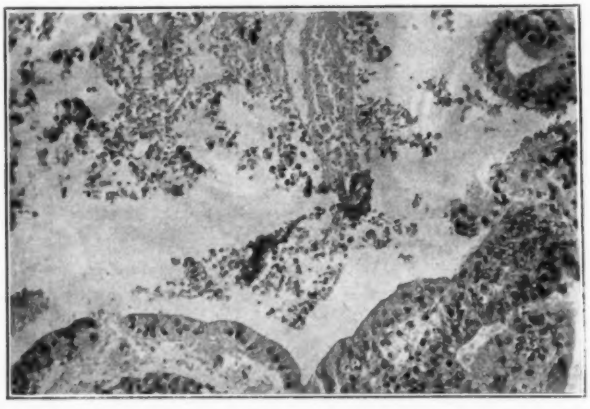

Fig. 2.—Photomicrograph of an explant seven days old. Considerable of the stroma is necrotic. There is a moderate hyperplasia of the surface and glandular epithelium. ×270.

lar leucocytes. In the deeper layers of the mucosa these cells may be numerous. An abundant supply of capillaries is distributed in networks under the surface epithelium and around the glands. The uterine glands are simple tubules lined by ciliated columnar epithelium. The variations during menstruation have been analyzed and described by Bartelmez.[6]

A study was undertaken to determine in serial sections the behavior of human endometrium explanted into a medium composed of human tissue fluids and to note especially any changes of the epithelium.

Uteri removed in the operating rooms were sent sterile to the laboratory and were kept for convenience at body temperature in an incubator not longer than one to three hours. Thin pieces of endometrium of 2 to 4 sq. mm. surface area then were explanted into a medium composed equally of heparinized (1:10,000) plasma obtained from postpartum women and tissue extract made by crushing endometrium in Tyrode's solution. The cover glass method of tissue culture described by Maximow[7] was used. The explants were transferred into fresh medium at intervals of one to three days. Certain cultures were useless because of contamination or failure to grow. The rapid liquefaction of the medium about the explants and the fragmentation of the newly-grown tissue cells in the liquefied medium were further difficulties encountered. Seven sets of cultures were endometrial explants from women twenty to thirty years of age; sixteen were from women thirty to forty years of age; eight were from women forty to fifty years of age; and one was from a woman sixty-five years of age.

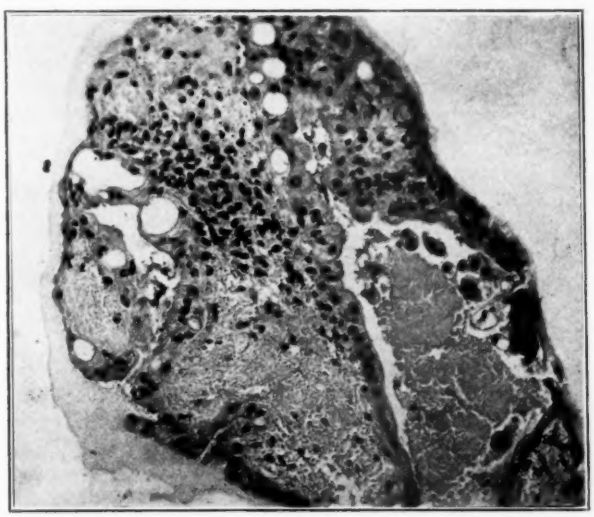

Fig. 3.—Photomicrograph of an explant fourteen days old illustrating the marked necrosis of the stroma tissues, the hyperplasia of the epithelium, and its orderly relation with the stroma. ×270.

Within twenty-four hours, as a rule, the medium about the explants was liquefied and a growth of tissue cells mainly of the polyblasts or lymphocytes of the stroma extended about the margins. The surface epithelium thickened into two or three cell layers and sometimes into small blunt sprouts. Some blunt sprouts broke away and formed small clusters of cells in the liquefied medium or stroma cells. The epithelium in the tubules thickened like that of the surface epithelium but without buds. Portions of the explants failed to grow; the loss by fragmentation in the liquefied medium and in the manipulations of transfer markedly diminished the mass of cells. Cultures surviving ten to fourteen days or longer were often reduced to dimensions of 1 or 2 mm. in diameter. When, fortuitously, the cells grew on the surface of the medium with a minimum of liquefaction, thin sheets of polyblast cells equalling several square millimeters dimension, grew in twenty-four to forty-eight hours. The fibroblastic stroma cells grew out along the edge of only a few cultures as stellate cells with long fibrils. The epithelium after thickening into several layers, became relatively stationary and did not extend in solid masses of cells into the medium. In fact, the relation of the epithelium to the stroma portions was maintained in the explants in an orderly way just as in the tissues of the endometrium in

vivo, with the exception of a slight hyperplasia. In a few explants, the growth of epithelium resembled that of an infiltrating carcinoma. This, however, was exceptional. The regeneration of epithelium in tubules from the basal layers was observed clearly in certain explants where the lining epithelium had desquamated. The desquamated epithelium of such tubules occupied the lumen; a lining of regenerated epithelial cells had replaced those lost. Epithelial cells in mitosis were observed more frequently in the younger cultures than in the older. Small mats of cotton fibers introduced into the mediums with the explants did not overcome the difficulties of tissue fragmentation. The epithelial cells in such cultures extended along the cotton fibers but thickened only into layers of two or three cells. Careful surface implantation of the explants made no appreciable difference in the growth of cells. Explants grown under anaerobic conditions survived only a few days. The growth of tissues in these cultures was not different from those grown aerobically. Glycogen granules were not found in the epithelial cells of explants surviving seven to twelve days.

COMMENT

The behavior of the epithelium in explants of endometrium from uteri of women during the childbearing years, introduced into a medium of human plasma and endometrial tissue extract, in some respects resembles but, in others, differs from that reported for the epithelium of embryos or young animals. Fischer's[8] monograph described a growth of epithelium in sheets on the surface of culture mediums following a short latent period. Groups of epithelial cells in these surface growths arranged themselves in rings which resembled cross sections of glands. Fischer, in old cultures, noted giant cells, retrogressive changes, and variations in the size and shape of the cells. He ascribed these to differences in the consistency of the medium or to the position of the explant in the medium. When the growth of epithelium occurred in membranes, according to Fischer, it was rapid and extensive, but when tubules formed, the rate of growth was much slower and the actual increase in mass was small. In some of Maximow's[7] cultures of the mammary gland of the rabbit, growths of epithelium resembling carcinoma occurred. Herzog's[9] recent review summarized the studies on the behavior of epithelium in explants. In general, his conclusions were the same as Fischer's.

The growth of epithelium in the human endometrial explants of our cultures was not in sheets but was limited to a hyperplasia of the cells into several layers and small buds. The epithelium of explants surviving ten to fourteen days or longer covered the stroma portions of the explant in an "organoid" way, as Maximow proposed. Explants that survived a month had a little of the original fibrillar stroma tissues and were covered by a single layer of large cuboidal epithelial cells.

These experiments demonstrate that the medium of human plasma and tissue extract prepared from human endometrium sustains life and promotes growth of the tissues in human endometrial explants at least a month, although after this time these activities are small. The tissues surviving this length of explantation are mainly epithelium. Maximow thought that various stimuli may have contributed to the carcinoma-like growth of epithelium noted in his cultures of the rabbit mammary gland.

These, he stated, were (1) mechanical, the trauma of tissues; (2) chemical, the presence of some constituent of the tissue extract; and (3) the potentials of the epithelium in the host before explantation, such as its state of activity, and individual and racial peculiarities. The medium used in the cultures of endometrium probably contained constituents which occur regularly in endometrium living in the human body. It should produce no greater stimulus than that taking place with the usual cyclic changes of the uterus.

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BILATERAL RENAL AGENESIS IN THE FETUS, ASSOCIATED WITH OLIGOHYDRAMNIOS

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COMPLETE absence of both kidneys is an anomaly of great rarity and is apparently always associated with oligohydramnios, in itself a phenomenon rarely encountered. The report of two cases is thus of great interest as a matter of record and, in addition, invites attention to the question of the function of the kidneys in fetal life and of the source of amniotic fluid.

Case 1.—Mrs. J. H., aged thirty, white, para ii, entered Harper Hospital at 2 P.M., September 22, 1930, a private patient of Dr. A. W. Coxon, for an elective cesarean section. A section had been done three years previously for placenta previa, followed by a prolonged convalescence from postoperative pelvic infection.

The last menstrual period was December 25, 1929. Estimated date of confinement October 1, 1930. Quickening at four months. In August there was bloody show for three days, with some uterine contractions. At the time of admission, the patient was not in labor. Physical condition good. Urine negative. Fundus of uterus 4 fingers below the xyphoid. Fetal heart regular, rate 130.

A classical cesarean section was done under spinal anesthesia, using 150 mg. of novocaine. Amniotic fluid was entirely absent. Breech presentation found. The fetus was pink in color and seemed fully developed, but did not breathe except for occasional spasmodic gasps. In spite of various stimulants regular breathing could not be established and the heart action ceased one hour after delivery.

Postmortem examination demonstrated a well developed and well nourished fetus, length 45 cm., weight 1985 gm. There were no deformities discernible by palpation or inspection. The internal organs were well developed and in their normal relationships except for the urinary system. In the position normally occupied by the right kidney lay a brownish kidney shaped organ 40 by 30 by 7 mm., weighing 4 gm. On the left side was a similar organ 45 by 30 by 7 mm., weighing 5 gm. These

proved to be suprarenal glands. By following down the remains of the urachus a rudimentary bladder with a rugous lining was found, whose internal surface measured 9 by 6 mm. The urethral opening into the bladder was present but there were no ureteral openings. No ureters, or structures resembling them, could be demonstrated. The testicles were in the scrotum.

The microscopic findings were not remarkable. The placenta appeared normal in the gross and in the stained section.

CASE 2.—Mrs. R. B., aged twenty-four, white, para iv, entered Harper Hospital far advanced in the second stage of labor at 9 P.M., November 7, 1930, as a private patient of Dr. H. C. Mack.

Fig. 1.—Dissection of abdominal cavity in fetus of Case 2. The suprarenals are readily seen as the large, thin ovoid bodies of the upper abdomen. Below the right suprarenal is the right testis supplied by a branch of the suprarenal artery. Just below the bifurcation of the aorta on the sacral promontory lies a small irregular fibrous mass containing scattered hypoplastic glomerular bodies and fetal type tubules (Fig. 2). From its lower edge a fibrous cord extends to a pea sized bladder which may be identified as a grayish body lying in the pelvis.

She had had 2 living children, followed by a stillbirth at eight months in June, 1929, the cause of which was not determined. The last menstrual period was January 21, 1930. Estimated date of confinement November 2, 1930. Quickening at four months. This patient was seen at regular intervals throughout pregnancy by Dr. Mack, the last examination being one day before entry. Nothing abnormal was noted at any time. Fetal movements were felt up to the onset of labor, which occurred a few hours before admission to the hospital.

Upon admission the fetus was presenting S.L.A. at the vulva, so delivery was done without further examination. A 2500 gm. fetus of good color was delivered which, however, did not attempt to breathe, rapidly became cyanotic and was pronounced dead ten minutes after delivery. Because of the appearance it was presumed that death occurred at, or shortly after the time of delivery, and not in utero. No amniotic fluid was noted at the time of delivery and the patient stated emphatically that none had been lost before or during labor although it was present in appreciable amounts in her three previous deliveries. The placenta was 10 cm. in diameter, and contained numerous infarcts.

Postmortem examination demonstrated a well developed and well nourished fetus, 49 cm. in length, weighing 2500 gm. There was an imperforate anus and the testicles were not in the scrotum. There were no abnormalities of the internal organs except

Fig. 2.—This represents a section taken from the fibrous mass on the sacral promontory. With considerable difficulty a field was found which contained a hypoplastic glomerular body. Scattered fetal type tubules can be seen.

those relating to the genitourinary system. In the position normally occupied by the kidneys were thin, brown kidney shaped organs weighing 4 and 5 gm. The bladder was found to be a very small organ with a small collapsed cavity from the base of which extended a duct through the prostate to a small, irregular, firm gland-like structure situated on the sacral promontory, which proved to be undeveloped kidney tissue. The testicles, with epididymis and vas deferens, were lying free just above the brim of the pelvis. The inferior vena cava existed as two trunks continuing upward from the iliac veins. The right hypogastric artery was absent and the left common iliac which gives rise to the left hypogastric artery was larger than the right. The rectum terminated at the base of the bladder but did not communicate with it (Fig. 1).

Microscopic examination revealed abnormal findings only in the lung, kidney remains and placenta. The lungs were completely atelectatic with deposits of hematoidin throughout the alveoli. The kidney remains consisted of a fibrous mass interspersed with fetal type tubules and an occasional hypoplastic glomerular body.

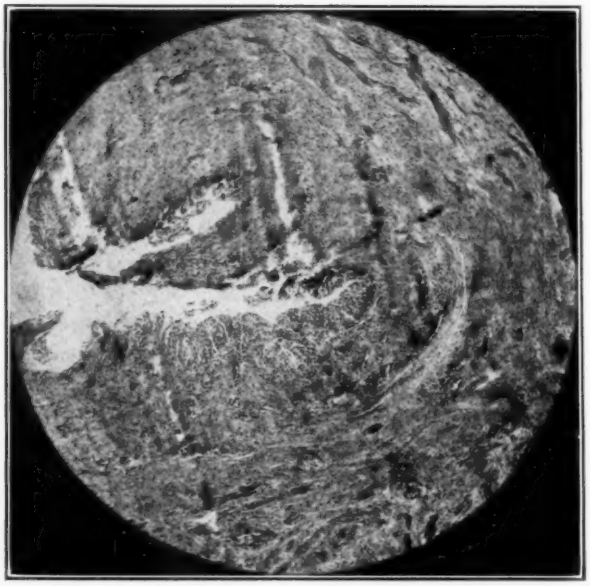

Fig. 3.—Cross section of the opened bladder showing the typical epithelial lining of the nearly obliterated cavity.

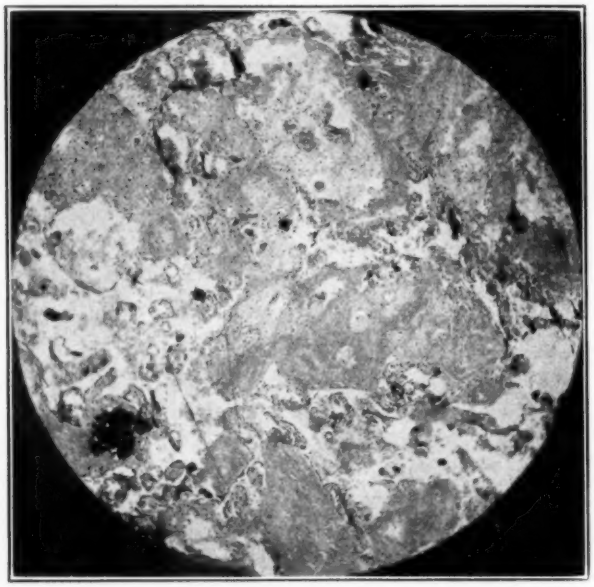

Fig. 4.—Placenta. Extensive infarction. No stigmata of infection.

The bladder and prostate were not remarkable. The placenta showed an unusual amount of infarction and calcification, but no evidence of infection (Figs. 2, 3, 4).

In five of the cases presented in Table I we may assume that the caudal portion of the nephrogenic cord failed to develop metanephrogenic tissue and coincidentally, no budding occurred at the lower end of the wolffian duct. In two cases ureteral budding did take place as evidenced by ureteral remains in the form of a fibrous cord in one and a small amount of eccentrically placed hypoplastic kidney tissue in the other. The defect in development then had its beginning at about the 5 mm. stage, or fourth week, at which time the mesonephros is most fully developed.

In 1921 Huerzler described a fetus with complete absence of both kidneys associated with oligohydramnios, and stated that search of the literature revealed only two similar cases, those of Hoenes and Hochsinger. However, Giles and Strassmann had each observed this condition and recorded a case previous to Hoenes and Hochsinger.

Table I presents all reported cases of bilateral renal agenesis including the two studied by the writer.

TABLE I. TOTAL REPORTED CASES OF COMPLETE AGENESIS OF BOTH KIDNEYS

AUTHOR	AGE SEX	VIABILITY AT BIRTH	LIQUOR AMNII	EXTRA URINARY ABNORMALITIES	ANOMALIES OF URINARY TRACT
Giles 1892	Term Male	Viable	No note made in case report	Imperforate anus, malformed feet, rectum and bladder, absence rt. hypogastric artery, undescended testes	Absence both kidneys and ureters
Strassman 1894	8 mo. Male	Viable	None	Bilateral club feet, undescended testes	Absence both kidneys and ureters
Hoenes 1895	Term ?	Viable	None	Compressed cervical vertebrae, club feet, closure posterior fontanelle	Absence both kidneys, rt. ureter present as a cord
Hochsinger 1899	Term ?	Viable	None	Bilateral club feet, dislocation of both hips	Absence both kidneys and ureters
Huerzeler 1921	Term Male	Viable	None	Undescended testes	Absence both kidneys and ureters
Author's case 1930	Term Male	Viable	None	None	Absence both kidneys and ureters
Author's case 1930	Term Male	Viable	None	Imperforate anus, absence rt. hypogastric artery, undescended testes, double inferior vena cava	Absence both kidneys. Small clump abnormal renal tissue on sacral promontory with duct to bladder

In addition to the above are several cases of hypoplasia of the renal system so complete as to leave no doubt of the nonproduction of urine. Academically they are to be distinguished from the cases of complete agenesis but from their association with oligohydramnios cannot be distinguished in considering the relation of fetal urine to the production of amniotic fluid. Table II outlines this anomalous condition and its associated features.

TABLE II. REPORTED CASES OF EXTENSIVE RENAL HYPOPLASIA WITH OLIGOHYDRAMNIOS

AUTHOR	AGE SEX	VIABILITY AT BIRTH	LIQUOR AMNII	EXTRA URINARY ABNORMALITIES	ANOMALIES OF URINARY TRACT
Jaggard 1894	Term Male	Viable	None	No rectum. Imperforate anus. Bilateral hip dislocation. Absence lt. sternocleidomastoid muscle	Absence left kidney and ureter. Small cystic rt. kidney, obstructed rt. ureter, and urethra
Hauch 1908	8 mo. Male	Viable	None	Undescended testes, double pes planovalgus	Bilateral kidney aplasia
Walz 1923	8 mo.	No note	None	Absence genitalia, cloaca present. Left club foot, polydactilia, umbilical artery continuous with aorta	Both kidneys a clump of pinhead sized vesicles. No urethra
Bardram 1930	8 mo. Male	Viable	None	Club feet	Absence rt. kidney and ureter. Lt. kidney enlarged, entirely cystic. Bladder pea sized, empty
Bardram 1930	8 mo. Female	Viable	None	Bicornate uterus	Kidneys low, small, hypoplastic. No lt. ureter. Bladder tiny, empty
Bardram 1930	8 mo. Male	Viable	None	Aplasia left tibia, micromelia left leg, one toe on left foot, spina bifida, imperforate anus, undescended testes	Bilateral kidney aplasia
Bardram 1930	8 mo. Male	Viable	None		

There are several observations of interest to be made on these two series as a whole, apart from the common urinary anomaly of the first group. Ten fetuses were males, one a female, in three this knowledge of the sex could not be obtained, and all were at or near term; all were viable at birth save one (no note) but lived less than one hour; in all but one there was a definite history of oligohydramnios, and in this case the

presence or absence of amniotic fluid was not indicated; associated deformities were malformed feet, malformed rectum and bladder, absence of rectum, imperforate anus, persistent cloaca, polydactilia, spina bifida, aplasia of the left tibia, bicornate uterus, compressed cervical vertebrae, closure of posterior fontanelle, dislocation of hips, undescended testes, and absence of the right hypogastric artery. In other cases of oligohydramnios, fracture and bending of long bones, and ichthyosis have also been observed. Some of these deformities, and many others such as harelip, are seen with normal and even excessive amounts of amniotic fluid, and Ahlfeld has even observed cases of ichthyosis with normal amounts of amniotic fluid. Certain of these deformities, as club foot, fracture and bending of long bones, compressed vertebrae, and possibly ichthyosis can be accounted for by mechanical influences following oligohydramnios. The others are developmental failures independent of the lack of amniotic fluid. From the fact that all fetuses were at or near term and viable at birth, it seems fair to assume that fetal kidneys play a negligible rôle in the physiology of the fetus, but by inference from the death of all fetuses shortly after birth, the kidneys must assume a major rôle immediately after being cut off from the maternal circulation, as do also the heart and lungs.

These 14 cases of renal agenesis and hypoplasia associated with oligohydramnios are of great importance when one considers the question of the source of amniotic fluid, for proponents of the fetal urine theory look for their greatest support in those instances of oligohydramnios associated with urinary anomalies. Considered alone these cases of complete renal agenesis, together with the cases of renal hypoplasia would seem to afford sound evidence in favor of this theory. There might also be added as evidence the fetus of Bertkau, full term, no amniotic fluid, and the urethra obstructed by a membrane which, when ruptured, allowed the escape of a half ounce of turbid urine; and Neumann's case of sirenomelus with renal agenesis and oligohydramnios.

Polyhydramnios not infrequently occurs in unioval twin pregnancy, affecting only one amniotic sac, and in these cases it is difficult to escape the conclusion that fetal urine has to do with overproduction of fluid. The twins as a rule differ markedly in size; the heart and lungs of the larger twin are greatly hypertrophied; the polyhydramnios affects the amniotic sac of the larger twin, that of the smaller twin containing a normal or a diminished quantity of the fluid. The umbilical vessels of unioval twins always anastomose freely in the single placenta and, if for some reason one twin obtains more than its fair share of the circulating blood, its heart and kidneys hypertrophy, with the result that the secretion of urine is greatly increased and polyhydramnios follows. Opposing this observation are the cases of Benthin who found practically the same sized kidneys in certain unioval twins despite great differences in the quantity of amniotic fluid. However, a careful review of the litera-

ture by Schiller and Toll in 1927 shows but 57 reported cases of oligohydramnios of which only 15 present malformations of the urinary tract, many of these 15 showing neither complete renal aplasia nor obstruction to urinary outflow, such as Schiller and Toll's case with left kidney and ureter absent, but right kidney compensatorily enlarged and with double ureter. Then again, Wagner has reported many cases of aplasia and atresia of the urinary system with normal and even excessive amounts of amniotic fluid.

Schiller and Toll studied carefully their case of oligohydramnios with an anomalous development of the urinary system, previously mentioned, and found a diffuse chronic inflammatory change with infiltration of leucocytes in the placenta, amnion, and chorion. The amniotic epithelium was nowhere degenerated and showed on its fetal surface only cuboidal and flattened forms which are described as normal for the middle of pregnancy. However, the vacuolated structure and drops of secretion which Forsell describes as characteristic for the normal amniotic surface, was nowhere observed, and the conclusion is drawn that histologically no ground can be found for attributing a secretory activity to the peripheral amniotic epithelium in this case. They believed that toxic products passing from the infected placenta directly into the amniotic sac must have altered the function of the secretory epithelium even if it did not destroy the epithelium, and on this basis explained the oligohydramnios. In the cases presented by the author no evidence whatever could be found of inflammatory changes in placenta or membranes.

That the oligohydramnios is not the cause of the renal agenesis is certainly true, especially in the light of Ahlfeld's statement that decrease or disappearance of the amniotic fluid takes place in the latter half of pregnancy, long after the embryologic defect has become manifest. That the oligohydramnios is the result of failure of adult functioning renal tissue to develop and not a coordinate phenomenon must remain a debatable question. The numerous cases of oligohydramnios with normal kidneys is clear evidence that they are not the decisive element in the production of the amniotic fluid. This fact is further borne out by those cases with a normal amount of amniotic fluid despite malformations of the kidneys or closure of the urinary passages. These cases of kidney malformations with normal amounts of amniotic fluid, on the one hand, and normal kidneys with oligohydramnios, on the other, speak against cause and effect, yet it is impossible to ignore the fact that 6 of the 7 cases of complete renal agenesis and all 7 of the cases of renal hypoplasia with absent renal function were associated with oligohydramnios, and in the seventh case of the former series the record is incomplete.

Further evidence from clinical observations to indicate a positive relationship between fetal urine and the production of amniotic fluid is to be found in a study by Bardram. He examined the postmortem records of all the cases of kidney anomalies found in children, either stillborn or dying shortly after birth, and who were autopsied at the Pathological-Anatomical Institute of Copenhagen from 1911 to 1929. This study was undertaken to see the relationship of kidney malformations in general to oligohydramnios.

He found: 7 cases of hypoplasia renum
2 cases of unilateral polycystic kidney
12 cases of bilateral polycystic kidney
4 cases of horseshoe kidney
12 cases of unilateral hydronephrosis
13 cases of bilateral hydronephrosis
2 cases of bilateral kidney aplasia
8 cases of unilateral kidney aplasia

By examining the hospital records of the births of these fetuses he found that oligohydramnios occurred in:

100 per cent of the cases of bilateral kidney aplasia
100 per cent of the cases of unilateral kidney aplasia with hypoplastic solitary kidney
67 per cent of the cases of bilateral polycystic kidney
43 per cent of the cases of hypoplasia renum
0 per cent of the cases of unilateral kidney aplasia with normal solitary kidney
0 per cent of the cases of unilateral polycystic kidney
0 per cent of the cases of unilateral or bilateral hydronephrosis

Bardram's study together with the 14 cases reviewed in this paper certainly make it reasonable to assume clinically, at least, that the fetal kidneys play some rôle in producing amniotic fluid though its exact nature is not yet known.

From another quarter comes more recent evidence, adduced from extensive physical and chemical studies of maternal blood serum, fetal urine and amniotic fluid, to give added weight to the inferences drawn from the clinical observations already discussed. Makepeace and coworkers were able to show that ". . . . at term the amniotic fluid is distinctly hypotonic to maternal serum, but in the earlier months of pregnancy this hypotonicity is less, and in the earliest months the amniotic fluid may be isotonic with maternal serum. Thus, early in pregnancy the amniotic fluid approaches the composition of other protein free fluids which are in osmotic equilibrium with the blood plasma. This suggests that the amniotic fluid originates as a dialysate in equilibrium wth the maternal and fetal body fluids. The fetal urine is definitely hypotonic and is present in the bladder as early as the fourth month in pregnancy. This indicates as pregnancy advances the amniotic fluid becomes more and more diluted by the hypotonic fetal urine."

The relationship of fetal urine to the production of amniotic fluid is further implied by a consideration of the embryologic development of the kidney in the light of observations made by three men. The metanephros or adult kidney is developed to the point of function somewhere between the third and fourth month of embryonic life. Makepeace was able to obtain urine from a fetus three to four months of age; Zangmeister concluded that as early as the fifth month of pregnancy the amniotic fluid must be diluted with an appreciable amount of fetal urine; and Ahlfeld states that the disappearance of the amniotic fluid takes place in the lat-

ter half of pregnancy. We may fairly assume that in the 14 cases presented amniotic fluid was present early in pregnancy, before the fourth month. At this time the metanephros failed in development and no urine was formed, following which the production of amniotic fluid ceased. If amniotic fluid were entirely a transudate from maternal blood, or a secretion of the amniotic epithelium, one would expect some fluid to have been present at term. Therefore another factor must be necessary, namely the presence of secreted fetal urine.

Schiller and Toll advance an enticing theory that the fetal kidneys produce only small amounts of a highly concentrated urine which, acting as an irritant, stimulates the amniotic epithelium to secrete fluid of low concentration. This theory may well explain the cases of complete renal agenesis associated with oligohydramnios, and their own case in which placental infection with its related inhibition of secretory function of the amniotic epithelium is well established, but it is difficult to apply to those cases of oligohydramnios in which no urinary anomaly occurred. However, even in those cases there may have been a pathologic condition in mother, fetus, or placenta either unobserved or unreported which altered function of either the amniotic epithelium or the fetal kidneys. Also, it is not incompatible with the view of Makepeace that amniotic fluid is originally a dialysate in equilibrium with maternal and fetal body fluids becoming more and more diluted by the definitely hypotonic fetal urine as pregnancy advances.

In conclusion it may be stated that oligohydramnios is rare; complete renal agenesis is extremely rare, but is apparently always associated with an absence of amniotic fluid; fetal kidneys play a negligible rôle in the physiology of the fetus except as they may relate to the production of amniotic fluid; and that these 7 cases of complete renal agenesis, 6 of which are associated definitely with oligohydramnios, together with 7 cases of extensive renal hypoplasia and oligohydramnios, afford presumptive evidence in favor of the view that there is a direct relationship between the production of fetal urine and the production of amniotic fluid.

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REPORT OF A CASE OF OVARIAN EMBRYOMA*

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REVIEWING the literature and our own cases I find that ovarian embryomas are not uncommon.

The terminology used for the classification of this form of tumor is very confusing. It has been called embryoma, teratoma, teratomatous, teratoblastoma, teratoid, dermoid, cystic and solid teratoma, mixed cell tumor, benign and malignant teratoma by various writers.

After an intensive study of this problem Willms[1] concluded that the dermoid cyst and teratomas of the ovary are genetically similar. They both contain all three embryonic layers. It was he who suggested the simple and anatomically correct term cystic and solid embryoma.

Out of 775 cases of ovarian tumors operated at the Ravenswood Hospital, fifteen cases of ovarian cystic embryomas were found. These were all unilateral tumors. The largest tumor in this series weighed two pounds. The youngest patient was twenty-three years old, the oldest sixty-four. One case of ovarian cystic embryoma with twisted pedicle was operated as a surgical emergency. There were no malignancies in this group.

Kroemer[2] found in his collected cases that thirty-four operations were performed with a primary mortality of 16 per cent. Out of 27 patients that recovered from operation, 16 or 59 per cent, died within the first or second year. Of 7 patients in this group that were considered cured, only 5 could be followed for more than five years, giving a curability of 25 per cent. Doderlein[3] gathered 51 cases in the literature. Twelve of this group were found well from six months to seven years after operation. He also found that only 4 cases were reported well after six to twenty-four years after surgical removal. Harris[4] collected 21 cases in the literature under the age of fourteen. The youngest girl of this group was under four. His own patient, five years and ten months of age, was found well ten years and eight months after operation. Eden and Lockyer[5] have gathered 16 cases of solid embryoma. The oldest patient in their group was thirty years old. Black[6] operated on two patients with solid embryoma of the ovary, one patient remaining well after three years and the other showing no sign of recurrence after fourteen months' observation. DeMora[7] has reported a patient of nine years of age having a large right ovarian solid embryoma. This case was operated by Gorst. There has been no recurrence in eight months.

Willms[1] considered the solid embryomas as originally benign, only secondarily showing malignant changes. Pfannenstiel,[8] Ewing[9] and Boyd[10]

*Presented before the Chicago Gynecological Society, March 18, 1932.

feel that these tumors are malignant from the very beginning. Secondary involvement occurs from the perforation of the capsule and implantation in the pelvis, peritoneum, diaphragm and omentum. Histologically, solid embryomata present lawless growth of varieties of tissues derived from the ectoderm, endoderm and mesoderm. Though it is common to find mostly organs and structures of the cephalic portion, yet intestines, solid abdominal viscera, muscle, bone, cartilage, nerve, etc., are found. Some observers found that in this type of tumor the mesoblast gains ascendency.

Studying the reported cases in the literature for some characteristic symptoms to aid in the diagnosis of this condition, one finds himself at a loss. The age of the patient and rapidity of the growth should always

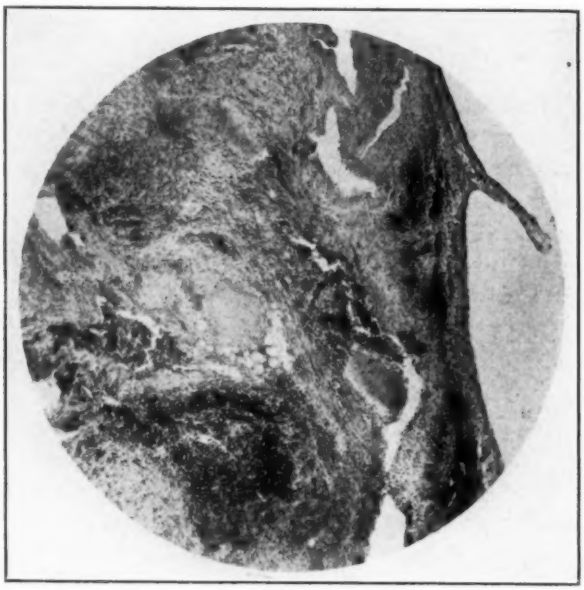

Fig. 1.—First tumor under low power ×52, solid embryoma.

bring solid embryoma to mind for differential diagnosis. Premature puberty with precocious somatic development has been reported by few observers.

Symptoms of pressure from the size of the tumor has been found in a majority of the cases. Ascites was usually present in young patients. Gardner[11] has pointed out that malignant tumors arising in a solid embryoma are usually mixed, carcinoma, rhabdomyomas or sarcomas, etc., depending on which elements partake in the malignant changes.

Case Report.—L. V., a girl, five years and four months old, was admitted under my care at the Ravenswood Hospital on January 7, 1930. Patient's chief complaint was of a rapid growing abdominal enlargement. Examination revealed that she was a normally developed girl whose past history was unessential except for a mild attack of measles when three years old. She had suffered from periodic attacks of vomiting since

childhood. These were generally brought on by nervous excitement. A presystolic murmur in the mitral region was present but the heart was otherwise normal.

About six months before consulting me, the child's mother noticed that the patient's abdomen was growing large with great rapidity. Examination revealed a very decided enlargement of the whole abdomen and on palpating, a firm smooth mass was found which extended from the ensiform cartilage to the symphysis pubis, towards the left side. The mass was somewhat fluctuant but not movable from side to side. The abdomen over the surface of the mass was dull to percussion. Pressure over the tumor elicited no tenderness but produced slight dyspnea. Absence of tympany over the abdomen indicated that the mass was external to the intestines. Putting the patient in the knee-chest position and palpating in the back, the possibility of a retro-(extra-) peritoneal tumor was ruled out. A series of roentgenograms made elsewhere was of no diagnostic help. There were no genitourinary symptoms present. No rectal or vaginal examination was made. Wassermann negative; hemoglobin 53 per cent; erythrocytes 4,160,000; leucocytes 16,000; small lymphocytes 21 per cent, polymorphonuclear neutrophils 79 per cent.

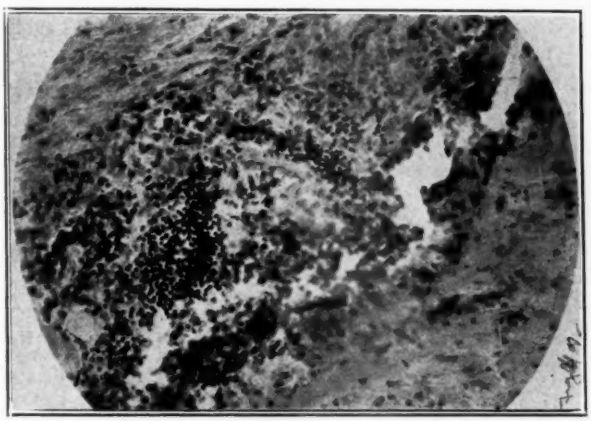

Fig. 2.—Same, under high power ×320.

A preoperative diagnosis of an ovarian tumor was made, though the location suggested a large cyst of the spleen which could not positively be ruled out without an exploration.

On January 8, 1930, under ethylene and oxygen anesthesia, a left paramedian incision with lateral retraction of the rectus muscle gave an excellent exposure of the tumor. The incision was four inches long and extended one and one-half inches above and two and one-half inches below the umbilicus. A large glistening tumor could be seen through the thin, almost transparent omentum. The multilocular tumor was not adherent to any neighboring structures. It was easily identified as a left ovarian growth and was removed intact by ligating the long vascular pedicle. The opposite ovary and neighboring organs were found normal. The abdomen was closed in the usual way, the operation lasting only forty minutes.

Aside from a slight rise in pulse and temperature for the first forty-eight hours, the postoperative course was perfectly smooth. The stitches were removed on the eighth postoperative day and the wound healed by primary intention. The patient left the hospital on January 19, 1930, twelve days after operation, in perfect condition. Our pathologist, Dr. L. C. Murphy, reported the pathologic findings of the tumor as follows:

"The specimen is a multilocular cystic tumor weighing 1370 grams (4.7 pounds) and measuring about 19 by 17 by 9 cm. The entire surface is smooth, glistening and in-

tact. Many of the cysts form projecting knobs on the surface. Some of the externally situated cysts are partially filled with thin, amber colored fluid but the greater portion of the mass is composed of compartments filled with edematous yellowish-white honeycombed tissue with lobulated appearance. In some compartments this tissue is firm and elastic while in others it is of a softer, semi-gelatinous consistency. Small calcified areas are noted in the solid, white tissue in some of the compartments. The microscopic sections show the structure of a teratoma in which the following tissues are represented: Cartilage, bone, muscle, fat, glands, ovarian stroma, squamous epithelium.''

The patient was kept under observation and was regularly examined every two weeks. The progress was found very satisfactory. Repeated abdominal palpation revealed no enlargement. On October 21, 1930, the patient was examined and showed very satisfactory results.

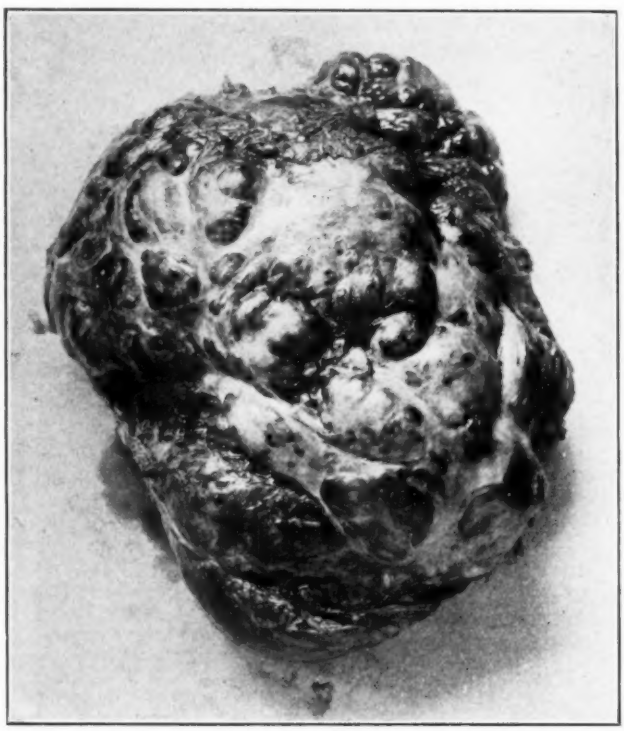

Fig. 3.—Second tumor removed Dec. 5, 1930, 5 pounds, anterior view.

On November 20, following the last inoculation of diphtheria antitoxin at the public school, the patient developed vomiting, chills, and high fever. Though the fever subsided within three days, the mother noticed a fullness of the child's abdomen. Thinking that it might be gaseous distention she did not consult me until the twenty-ninth of November, exactly nine days after the inoculation of the antitoxin. The mother stated that ''the abdomen grew larger every day.'' I found the abdominal measurement showed a growth of five and one-half inches in the level of the umbilicus since the last examination. The mass was smooth and firm in palpation. It was much harder than the first tumor. The tumor filled the whole abdomen and the exact relation of it could not be clearly outlined. General examination indicated that the patient was in excellent condition for operation. The urine examination was negative except for a very faint trace of albumin. Blood picture showed hemoglobin 75 per cent, erythrocytes 4,220,000, leucocytes 11,750.

The patient entered the Ravenswood Hospital on Dec. 4, 1930, and was operated on under ethylene and ether on Dec. 5, 1930. The tumor was reached through the old scar. Some free bloody fluid was found on opening the abdomen. A large solid tumor filled the abdominal cavity. Its anterior part was attached to the greater omentum. This was easily ligated and separated. Three inches of ileum were attached to the posterior central part of the tumor. It was not possible to separate

Fig. 4.—Second tumor under low power. Adenocarcinoma ×52.

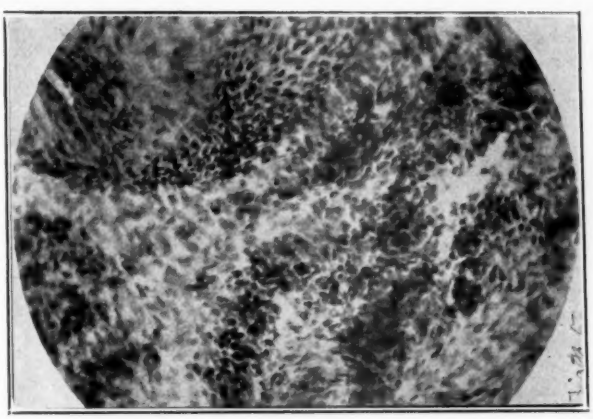

Fig 5.—Same, high power ×320.

the intestine without entering the tumor tissue, so six inches of the ileum were resected. A lateral anastomosis established its continuity. The abdomen was closed after a careful survey of the neighboring structures. No pathology could be found in the right ovary. No metastases were visible or palpable. The operation lasted one hour and twenty minutes.

The patient's rectal temperature rose to 103° F. for six hours after the operation. There was a normal bowel movement on the third postoperative day. Convalescence

was uneventful. Sutures were removed on the eighth postoperative day. There was primary healing of the wound. The patient left the hospital in excellent condition on the tenth postoperative day. The pathologic report by Dr. Murphy was as follows:

"The specimen is a round, solid tumor mass weighing five pounds. The external surface is smooth, of a dark mottled color with nodular irregular, bulging areas ranging in size from a walnut to an orange. The interior is composed of soft, edematous, yellowish-white tissue which becomes mottled with hemorrhage near the surface. Microscopic sections show practically the same structure as the tumor removed in January, 1930, viz., teratoma, except that in this second tumor there is a greater proportion of glandular epithelium indicating a more malignant structure (adenocarcinoma)."

The patient's convalescence was satisfactory for about three months after the last operation. On March 30, 1931, fluid accumulation in the abdomen was noticed. Enlargement of the right cervical glands was present. The patient became quite anemic and markedly debilitated. The intraabdominal fluid grew rapidly and it was necessary to remove one gallon of it, on May 14, 1931, to relieve respiratory embarrassment. Large abdominal mass, and the enlargement of the liver could be palpated at this time. The patient grew weaker and died on May 21, 1931.

Autopsy was refused.

Summary and Conclusion.—1. Ovarian embryomas are subdivided into cystic and solid types on anatomic grounds by Willms. This is the least confusing terminology.

2. The cystic embryoma is a common form of ovarian neoplasm. In a series of 775 ovarian tumors at the Ravenswood Hospital, 15 were cystic embryomas. This is a much lower percentage than found in other clinics.

3. The solid embryoma is a very rare ovarian tumor. It is malignant from the very beginning. A case of this type is reported in a girl of five years and four months of age. The tumor occurred in the left ovary and weighed 4.7 pounds. This was removed intact without difficulty. It recurred after eleven months. The tumor grew rapidly and filled the abdomen within nine days. Operation revealed a five-pound tumor originating in the greater omentum. The close adhesion to the ileum required a resection of six inches of the bowel. A lateral anastomosis established the continuity of the intestine. Postoperative recovery was satisfactory. The patient died within six months after the last operation from recurrence and metastasis.

4. Every solid embryoma should be considered potentially malignant. The study of the literature impresses the necessity of prophylactic removal of all ovarian cysts in toto.

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DISCUSSION

DR. LYMAN C. MURPHY.—I have seen two instances in which microscopic sections were made and a report given that no evidence of malignancy was found. In one case the pathologist even suggested a favorable prognosis and did not think x-ray was necessary. Both patients were dead within one year.

DR. IRVING F. STEIN.—The point brought out in reference to the malignancy of embryomas is important. The essayist said that they had had no experience with x-ray in the diagnosis of these tumors. I feel that they have missed something vital in the diagnosis. The large tumors, whether they be teratomas or cysts, indicate surgery from the size alone. The small growth from 2 to 4 cm. in diameter are very important from the standpoint of preoperative diagnosis and from the standpoint of whether or not they are to be attacked surgically. Our experience with the use of pneumoperitoneum in diagnosis is that we can detect many small ovarian tumors quite early and can differentiate various types of ovarian swellings by x-ray. Simple cysts, parovarian cysts and dermoids are readily distinguished, the latter by the presence of teeth, bone or small areas of calcification. We have shown that ovarian pathology can be visualized on the roentgenogram after pneumoperitoneum and thus determine whether operation shall or shall not be done.

DR. N. S. HEANEY.—Solid embryomas are so rare that single case reports are of the utmost importance. The condition of the remaining ovary at the time of the second operation in Dr. Sarma's case should be very definitely stated. Ovarian tumors are very frequently bilateral and when a patient has been operated upon for a tumor of one ovary and subsequently has to be operated upon for a second tumor the probabilities always are that the second ovary is also the seat of a tumor.

One point in the treatment of dermoids that I consider of some importance is that when one ovary is operated upon for a dermoid cyst the opposite ovary, though normal in appearance, should be carefully slit and inspected for the presence of a possible dermoid. If this is done one may occasionally find a dermoid no larger than a pea or bean which may be easily removed and prevent an operation at some future time when it has grown big enough to produce symptoms.

DR. DETARNOWSKY then stated that the right ovary was entirely normal, there was no pathology in the pelvis. He continued: The thing that puzzled us was to find out how there had been an implantation. At the first operation the original tumor was free of all adhesions. It was lifted outside without rupturing any of the cysts and was clamped without any difficulty at all and we could not see any signs of implantation anywhere. The child was normal all these months so that we felt that we had removed everything, and then she had this relapse. However, the opposite ovary had nothing to do with the second growth.

DR. ARTHUR H. CURTIS.—Do you not believe, in view of the serious prognosis, that it would usually be wise to give deep x-ray therapy to take care of the other ovary?

DR. DETARNOWSKY.—That is a good suggestion.

DR. FREDERICK FALLS.—I would like to recount a few interesting tumors of this type that I have encountered. The first was a large demoid cyst in the pelvis of a woman on the medical service of the University of Iowa, who had entered with a diagnosis of chronic rheumatism. The medical men could not find any focus of infection, except a mass in the lower abdomen which they took to be a pelvic abscess. This mass was opened and drained in July. Two months later the woman was still draining from the ovarian cyst and when I took over the service they told me there was a peculiar drainage from the vagina. We found on examining the vagina carefully that the interior of the cyst was full of maggots. During the hot summer flies had gotten in the

vagina and laid their eggs in this cyst. Since it was necessary to remove this dermoid, I took cultures from the cyst and found streptococci, staphylococci and colon bacilli. The woman was not a good surgical risk and yet because of the persistent discharge something had to be done to relieve her. We irrigated the cyst from the vagina thoroughly with weak iodine solution over a period of two weeks and reduced the number of bacteria. We then removed the cyst wall abdominally. After a rather stormy convalescence she recovered.

About three months ago a nurse, nineteen years old, was found to have a tumor about the size of a fist in the region of the ovary. I felt it should be investigated with the possibility that it might be a teratoma. She did not respond to the suggestion at once. Three weeks later the tumor was about twice the original size. I insisted that it should be removed at once and this was done. We found a teratoma. Feeling that, when we are dealing with a malignant tumor of the ovary, it is the general rule that the other ovary and uterus be removed, I removed the ovary and uterus from this girl.

About two years ago at the Research Hospital a girl about sixteen years of age was sent in with this history. She noticed a swelling of the abdomen. She told her mother about this and her mother took her to the family doctor who considered the possibility of a pregnancy. An x-ray picture was taken by a local dentist who said that the girl was pregnant. The father of this girl, on learning this, sent her to a reform school. The doctor in charge of this school looked her over and watched her for a month or two. The abdomen was growing about the rate a pregnancy would, but the heart tones could not be heard. The patient was then sent to the Research Hospital where we made a diagnosis of teratoma and found this at operation.

At the County Hospital about four years ago Dr. Schmitz did a hysterectomy with a right salpingo-oophorectomy. He did not remove the left ovary. Six months later the woman came in with a tumor in the region of the left ovary. I made a diagnosis of simple cyst, opened the abdomen and found a teratoma. Within six months after leaving in what appeared to be a normal ovary there had developed a teratoma.

Three years ago I took out a large cyst in an eighteen-year-old girl. This was a very rapidly growing cyst and proved to be a teratoma. All of these cases were malignant.

KRAUROSIS VULVAE, WITH A REPORT OF THIRTEEN CASES

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(From the Gynecological Service and Division of Laboratories of the Mount Sinai Hospital)

KRAUROSIS is an atrophy of the vulva due to changes in the epithelial and subepithelial elements of the skin. It usually occurs in women past the menopause, but may occur in young women. Its etiology is not well understood. Lack of ovarian hormone is considered a factor because it usually occurs in the seniium and there have been several reports claiming good results following the administration of female sex hormone. In the cases here presented, female sex hormone gave temporary relief in a very few instances and in no case changed the clinical or local condition. From this it may be inferred that the female sex hormone is not the important factor. Furthermore, while this disease is not rare, its incidence is very low even among the women who are past the climacteric. It is possible that an endocrine factor is the

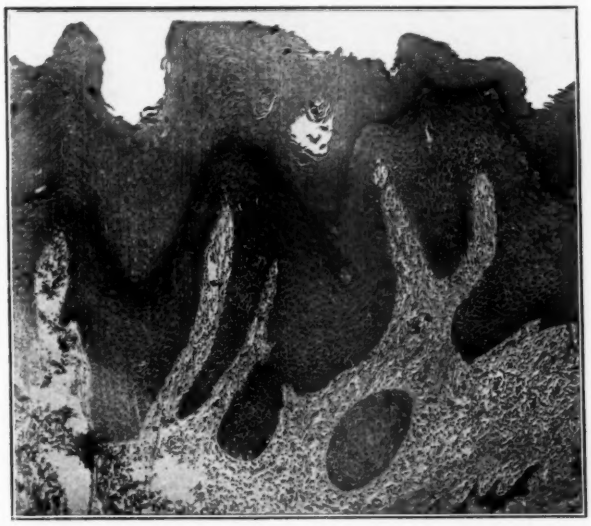

Fig. 1.—Marked acanthosis and heaping up of the keratin layer. Eleiden granules stain deeply and connective tissue shows chronic inflammation.

Fig. 2.—Labia majora are flattened out and the labia minora have completely disappeared. The clitoris and prepuce are shrunken and the vulval orifice contracted so that it barely admits finger tip. Skin has the appearance of thin parchment and is pearly white.

cause, but the proper one has as yet not been determined. Veit believes that kraurosis is of inflammatory origin of long standing.

In the last decade, cancer prevention and early recognition have received widespread interest. Carcinoma of the vulva comprises 4 per cent of all carcinoma of the genital tract. Berkeley and Bonney state that the relationship born by leucoplakic vulvitis to carcinoma is closer than that of any other pathologic lesion with the exception of roentgen ray dermatitis.

The clinical and histologic picture of kraurosis vulvae is a typical one. Early in the disease (Taussig's first stage) the vulva appears swollen and reddened (kraurosis rouge of Jayle). Histologically, there is a pronounced acanthosis, an increased keratosis and an infiltration with

Fig. 3.—Low epithelial layer. Papillary processes are absent, eleiden granules sparse, connective tissue densely collagenous, and there are islands of round celled infiltration.

round cells and leucocytes. The second stage usually begins about one year after the initial appearance of the disease. The skin becomes white and firm and there may be excoriations from scratching. Microscopically (Fig. 1), there is still a marked acanthosis and heaping up of the keratin layer. The eleiden granules stain deeply, the connective tissue shows chronic inflammation with scattered areas of collagen and numerous plasma cells. This is called the progressive stage by Szasz and Veit. In the third stage (Fig. 2), the labia majora flatten out, the labia minora completely disappear, the clitoris and prepuce are shrunken and the vulval orifice contracts so that it barely admits the finger tip. The skin assumes the appearance of thin parchment, is pearly white, dry and cracks easily. This condition may at times involve only one area of a labium or be unilateral. The microscopic picture (Figs. 3 and 4), shows

a low epithelial layer. The papillary processes are absent, eleiden granules are sparse, the connective tissue is densely collagenous and there are islands of round cells. The elastic tissue (Fig. 5), is decreased in

Fig. 4.—Higher power of Fig. 3 showing densely collagenous connective tissue.

Fig. 5.—Elastic tissue stain showing elastic tissue broken up and arranged as bundles of twigs.

amount and appears broken up and arranged as bundles of twigs. This stage of kraurosis corresponds to what Szasz calls kraurosis sensu strictori.

The most common symptoms that finally influence a patient to seek relief are pruritus and dyspareunia. Dysuria and frequency may also occur. These symptoms should be differentiated from other causes such as parasitic diseases of the vulva, diabetes, dermatologic lesions, and psychoneurosis.

The tabulated results of treatment of the thirteen cases of kraurosis vulvae studied may be divided into two groups (Table I). In Group I, there are five cases gathered from the out-patient and radiotherapy departments. They are all parous women past the fourth decade of life. Only one of these was still menstruating. In each case the symptoms and vulval lesions were characteristic of kraurosis. In three cases, low voltage x-ray was used without relief. In one, the Kromayer lamp was used, but the full course of treatments was not completed as the patient failed to return. Three of these patients received ovarian hormone, in the form of amniotin pessaries. In one, four suppositories a day were given over a period of two and one-half months without improvement.

In Group II (Table II), there are eight cases of kraurosis vulvae, in all of whom vulvectomy was finally done. Their ages ranged from twenty-nine to sixty-five. The twenty-nine-year-old woman had never menstruated and showed no sex hormone cycle in her blood. The thirty-eight-year-old patient had a hysterectomy performed four years before. Of these cases only one was sterile, the patient with the primary amenorrhea. They all complained of pruritus and in three dyspareunia was the chief complaint. Female sex hormone or x-ray, or both were used in all cases but one. In every instance, the results were poor. At best, these patients had temporary relief, but in no case was there any effect on the local condition. In one patient, no previous treatment had been given as it was deemed inadvisable to temporize because of the marked fissuring of the kraurotic skin. It is this case that shows a very early carcinoma with kraurosis in the hyperplastic phase (Fig. 6). Six blocks cut one-eighth inch in thickness, adjacent to that showing malignancy, failed to demonstrate the carcinoma. This emphasizes the importance of cutting many blocks from a kraurotic vulva specimen submitted for examination. The eighth case had a superimposed eczema of the vulva which masked the kraurotic appearance of the skin. The kraurosis became evident after local treatment for the eczema. Here also the microscopic finding of an early carcinoma on a kraurotic basis was unexpected. The results in 6 of the patients in Group II were most striking following vulvectomy. Five are cured for from three to five years. The sixth and eighth case have recently been operated. The seventh case, in whom there is a recurrence, was a private patient, not on the service of the hospital.

TABLE I. NONOPERATED CASES

PATIENT	AGE	MENSTRUAL HISTORY	PARITY	SYMPTOMS	DURATION	TREATMENT	RESULT	CLINICAL PICTURE
J. B. 318 159	69	Menopause 16 years	8	Pruritus Diabetes	7 years	12 amniotin pessaries, Kromayer lamp 4 doses	No relief, treatment incompleted	Both labia minora white, slight scaling, skin atrophic
S. M. 14 448	73	Menopause 25 years	6	Pruritus	5 years	Low voltage x-ray	No relief	Leucoplakia, fissures
R. G. 319 246	43	Operated for ovarian tumor, 1910. Menses regular 14x28x7	3	Pruritus	3 years	Low voltage x-ray	4/29/30. Is relieved before and during menses	Atrophic labia minora with leucoplakia and fissures
E. G. 17 087	58	Menopause 6 years	8	Dyspareunia Pruritus	6 years	Daily ½ c.c. of estrogen, P.D. for 7 days	No improvement	Atrophic labia minora, loss of clitoral folds, grey white appearance
I. W. 24 901	54	Menopause 14 years	5	Pruritus	3 years	4 amniotin pessaries per day for 2½ months, x-ray	No relief No relief	Atrophic labia minora, whitish in color

TABLE II. OPERATED CASES

PATIENT	AGE	MENSTRUAL HISTORY	PARITY	SYMPTOMS	DURATION	TREATMENTS	RESULT	OPERATION	PATHOLOGY	RESULTS
D. M. 331 930	29	Never menstruated	0	Dyspareunia Pruritus	2 yr.	Injection F. S. H. for 3 months, 3 R. U. per dose	Vulva unaffected. Temporary improvement	Vulvectomy 1926	Atrophic stage	Cured. Last seen 11/1/31
E. K. 277 615	65	Menopause 15 years	7	Pruritus	3 yr.	8 injections of amniotin, 50 R. U. per dose. 2 courses of low voltage x-ray	No effect No effect	Vulvectomy 3/18/27	Atrophic stage	Well
C. R. 288 613	48	Menopause 3 years	3	Pruritus	1 yr.	Injection F. S. H. for 4 months, 3 R. U. per dose	Temporary improvement. No effect on vulva	Vulvectomy 3/15/28	Atrophic	Slight itching following vulvectomy. Relieved by injections of theelin, 250 R. U. for 1 month. Last seen 10/28/31, well
I. A. 302 578	47	Menopause 5 years	2	Dyspareunia Pruritus	3 yr.	8 theelin injections of 50 R. U. per dose. X-ray pituitary, x-ray vulva	No relief No relief No relief	Vulvectomy 5/27/29	Hyperplastic stage	Last seen 9/17/30. Slight itching to right and posterior to vulva
I. H. 332 358	54	Menopause 5 years	9	Dyspareunia Pruritus	6 yr.	8 theelin injections of 50 R. U. per dose. X-ray pituitary, x-ray vulva	No relief No relief No relief	Vulvectomy 11/10/31	Atrophic phase	
A. B. 289 342	38	Menopause 4 years, post-hysterectomy	5	Pruritus	10 yr.	Low voltage x-ray	No relief	Vulvectomy	Atrophic	Pruritus. Not seen by us
C. G. 288 369	65	Menopause 25 years	1	Pruritus	2 yr.	None		Vulvectomy 2/7/28	Early ca. in kraurosis. Hyperplastic phase	11/1/31, skin healthy. Vagina admits 2 fingers. No glands
D. G. 32466	57	Menopause 9 years	4	Pruritus	2 yr.	Low voltage x-ray and local treatment	No relief	Vulvectomy	Early ca. in kraurosis	

Taussig, in his analysis of 76 cases of carcinoma of the vulva, found that 39 were on a kraurotic basis, 60 per cent being in the leucoplakie stage and 40 per cent in the atrophic stage. In other words, about 50 per cent in his series showed kraurosis in either stage.

The microscopic slides and clinical description of 13 cases of carcinoma of the vulva from Mount Sinai Hospital have been studied. In 7 there

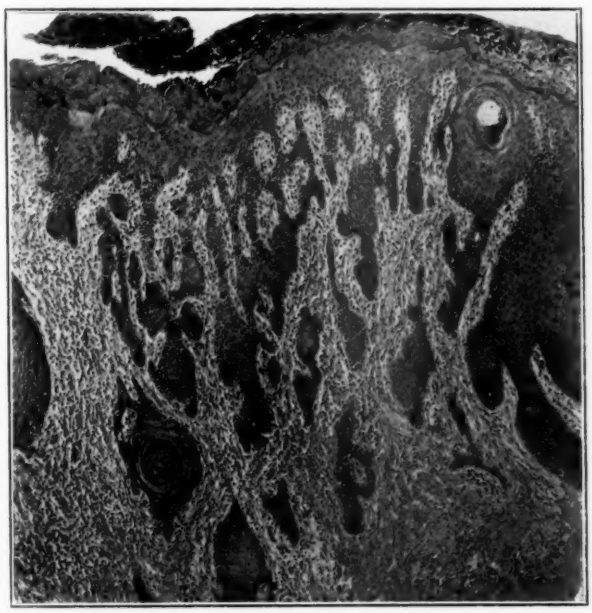

Fig. 6.—Early carcinoma, pearl formation and infiltration of connective tissue in a hyperplastic kraurotic lesion.

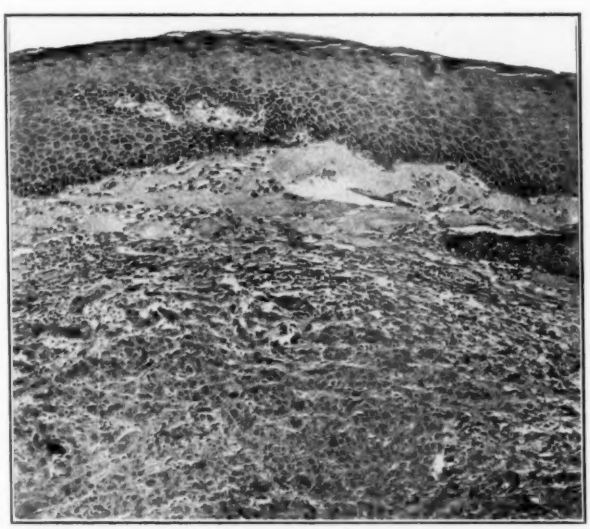

Fig. 7.—Advanced carcinoma in a kraurosis in the atrophic phase. Same lesion contains areas of kraurosis in hyperplastic phase.

was a coexisting kraurotic process (Fig. 7). They could not be grouped in the hyperplastic or atrophic stage because most of them showed both stages in the same specimen. The percentage of kraurosis in the carcinomas of the vulva studied corresponds to Taussig's figure of 50 per cent. This high percentage of carcinoma associated with kraurosis and the poor results with medical and physical therapy leads to the conclusion that the method of treatment should be vulvectomy. Brettauer, Frank, Taussig, and many others have stressed the importance of vulvectomy for prompt relief and cure of kraurosis vulvae. It is here further emphasized that to cure kraurosis vulvae and forestall carcinoma, vulvectomy should be done.

SUMMARY AND CONCLUSIONS

1. Thirteen cases of kraurosis vulvae are analyzed, of which 8 were treated by vulvectomy.

2. Thirteen cases of carcinoma were studied in order to determine a relationship to kraurosis.

3. Both from the literature and this analysis, carcinoma was found to develop in kraurosis in 50 per cent of the cases.

4. Unsuspected carcinoma was present in 2 of the 8 cases treated by vulvectomy.

5. X-ray and hormonal therapy is ineffective.

6. Vulvectomy is the treatment for cure of kraurosis and prevention of carcinoma.

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145 WEST 86TH STREET.

ON THE SUPPORTS OF THE UTERUS

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A CRITICAL review of the value of the ligaments as supporting structures to the uterus must result in the conclusion that they cannot be very effectual. This is especially true of the round ligaments, because at laparotomy it is seen that the uterus can easily be retroverted without any strain on the former and that the return of the uterus to its normal position upon the release of the retroverting strain is not due to their pull. This was well demonstrated in experiments performed by Mackenrodt[4] in which he resected a piece of both round ligaments near their attachment to the uterus in a manner to prevent the subsequent union of the separated muscular ends. He then retroverted the uterus and packed the intestines on its anterior surface, after which the abdomen was quickly closed. When the uneventfully recovered patient was discharged, he found that the uterus was in a normal position, even though during the convalescence the patient had been lying on her back, and of course, no longer had an intact round ligament to hold the uterus upward. The history of the end-result of round ligament operations for the cure of prolapse is also eloquent testimony of the ineffectiveness of these structures to support the uterus. The peritoneal folds forming the broad ligaments, because of their very structure, are not worthy of any consideration as uterine supports. The uterosacral ligaments composed of material similar to the round ligaments are of no more value as supporting structures than are the round ligaments. The only other structure possibly capable of supporting the uterus is the uteropelvic ligament, the Mackenrodt ligament, the cardinal ligament, or the infundibulopelvic ligament, as this structure has been variously called. Mackenrodt, in the examination of the fascia endopelvina (that portion lying over the levator ani and directly under the peritoneum) in a newborn, reported thick, bandlike fibers running directly to the vagina, rectum, and bladder in which were muscular elements. Dorsally, he found a mass of these fibers arranged like a band in the border of the broad ligament, but distinctly separate from it, running from the pelvic fascia into the cervix. This he designated the ligamentum transversum colli, and claimed for it the sole support of the uterus. According to him, in the fetus and newborn, it runs from near the last lumbar vertebra downward toward the side wall of the cervix to which it is attached. As the ilia develop, the ligament moves farther away laterally from the vertebral column, until it finally comes to lie in the transverse diameter of the pelvis. At its upper border runs the uterine artery.

He also described other bands of musculofascial fibers. One set of these forms the uterosacral ligaments and the other set the pubovesico-

uterine ligaments which latter run from the attachment of the ligamentum transversum colli to the cervix along the side wall of the bladder to the hind wall of the symphysis. Still other bands run out into the recto-vaginal and vesicovaginal septae, offering strong supports to the rectum and bladder and serving to close the pelvic floor aperture. All of these bands are attached through the ligamentum transversum colli to the uterus which is the pivotal supporting structure. These bands hold up the bladder and other pelvic organs.

These statements have been accepted for face value quite generally without being corroborated by investigation.

The adoption of original contributions as the fundamental basis for further work without research into the former for confirmation has been one of the greatest obstacles scientific progress has had to contend with.

In this instance the adoption of Mackenrodt's view has resulted not only in the development of a nomenclature but also in the elaboration of hypotheses regarding the mechanism of prolapse, cystocele, and rectocele. Many operations were developed for the cure of these conditions, adopting as fundamental, the existence of these ligaments and fascia as Mackenrodt described them. Thus it is quite common to hear operators speak of "operations for the correction of prolapse, cystocele, and rectocele, including the plication of rectovaginal fascia, vesicovaginal fascia, 'Mackenrodt's' ligaments, etc."

In 1910 Blair Bell[2] taught that the pelvic fascia instead of being a very complicated structure with a great many diverticuli accessory to the main portion, consisted of simply a fibrous tissue investure forming the sheath of and giving attachment to, the various muscles of the pelvic floor. Unfortunately however, his teachings did not receive the wide recognition that they deserved. Quoting from him, "Care must be taken that the separation is effected in the plane between the bladder wall and the muscle and fascia underlying the vaginal mucosa, not only in order that the separation may be easy but also that the muscle and fascia may be sutured together subsequently." This appears in the discussion on the technic of anterior colporrhaphy. Spaulding[6] in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, writing on hemostasis in vaginal hysterectomy presents photomicrographs of tissue between the bladder and anterior wall of the vagina, in which he very definitely speaks of a vesicovaginal fascia.

Recently Goff,[3] in an histologic study of the perivaginal fascia in a nullipara concludes that (1) there is no fascia of any kind in the walls of the vagina, urethra, bladder, or rectum; (2) there is no fascia between the anterior vaginal wall and the urethral wall; (3) there is a loose areolar fascia between the vagina and bladder and between the vagina and rectum not dissectable as a distinct layer; (4) this is the only fascia available to accord with the descriptions of fascia used in various operative procedures for the cure of cystocele and rectocele; (5) this "fascia" is not at all comparable with the dense fascia such as forms the sheath of the rectus abdominis.

In Goff's very interesting article, he states that a careful search through the literature had failed to reveal any previous attempt at a study of a similiar nature with the exception of that by Spaulding on sections from the vesicovaginal septum in which the latter failed to state whether the

subject from whom the material was taken was nulliparous or multiparous. It would seem that the more important point to make was that Spaulding disagreed with Goff's findings, inasmuch as he stated very definitely that there was a vesicovaginal fascia of a well defined character which he utilized in the performance of a certain portion of the operation of vaginal hysterectomy. To us it seems that the question of multipara or nullipara is of importance in the direction opposite to that taken by Goff, inasmuch as the practical value of any fascia in the vesicovaginal or rectovaginal septum, if such existed, would be found in its utilization in operations in multiparous women for repair of pelvic floor injuries. In other words if there was any such fascia existent, it would be much more important to find this in a multiparous individual who needed perineal reparative work than in a nulliparous woman who needed no operative procedure.

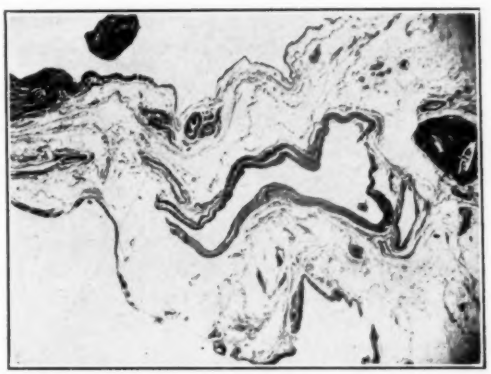

Fig. 1.—Fibrous tissue along the junction of cervix and uterine body in which is seen a longitudinal section of the uterine vein and a cross-section of the uterine artery just before it turns to course along side of the uterus. There is no ligamentous or fascial structure in this loose areolar connective tissue.

Dougal Bissell[1] in an article entitled "Fascial lapping as applied to the tissues of the vaginal wall, a misnomer" states that in cases of vaginal prolapse there is no definite fascial layer of the vaginal wall which can be isolated and used surgically to advantage. He presents photomicrographs of a section of tissue removed from the left side of the anterior vaginal wall. His conclusions are open to the criticism that the section of tissue which he examined was not a complete section of the vesicovaginal septum and that in the tissue remaining in the septum and not excised for examination, fascial tissue might have existed.

In our studies on the mechanism of the development of prolapse, among other things, we examined the structure of the vesicovaginal and rectovaginal septa.

Microscopic examination of sections of the vesicovaginal septum and the rectovaginal septum in autopsy material in a multiparous woman, showed no evidence of existence of any fascial structure comparable to that de-

scribed in any of the texts, in other words our findings are in thorough accord with the findings of Goff in his nulliparous material. In our operative material we have never been able to demonstrate any fascia in the rectovaginal or vesicovaginal septa. The only tissue to be found there, other than the mucosa is a loose, areolar connective tissue which can have no restraining or supportive value. Where then are those dense musculofibrous bands coming from the attachment of the ligamentum transversum colli or uteropelvic ligament as others call it, and spreading out through the vesicovaginal and rectovaginal septi of which Mackenrodt wrote?

In a similar set of studies made on autopsy material we investigated the tissue around the uterine arteries in their course from the internal iliac to the uterus in search for the so-called Mackenrodt ligament, and here again we met with negative results.

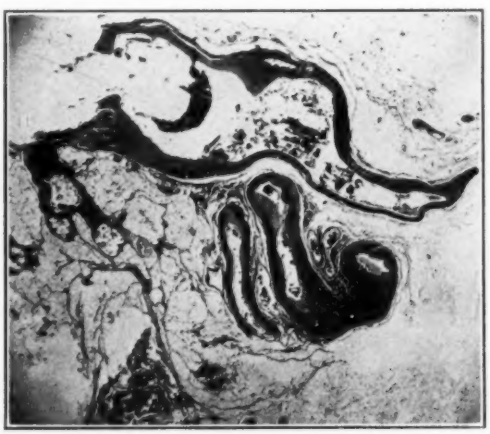

Fig. 2.—Cross section of the uterine artery, a longitudinal section of the uterine vein and a cross-section of two of its larger tributaries, and also a cross-section of the ureter with surrounding loose areolar connective tissue but no ligamentous or fascial tissue.

METHOD

The uterus, adnexa, bladder, vagina, and urethra and all the loose areolar connective tissue making up the parametrium were excised from a multiparous female patient, thirty-one years of age with no sign of prolapse or retrodisplacement of the uterus, and the entire mass was fixed in formalin for a week. Then sections were made of the rectovaginal septum and the vesicovaginal septum. A section was made longitudinally parallel to the uterine artery as it coursed along the uterus, beginning at the round ligament and extending downward as far as the junction of the vagina with the cervix, taking in a portion of the bladder wall and making a transsection through the uterine artery after it had curved away from the uterus out toward the lateral pelvic wall. This section contained all the loose cellular and fibrous tissue around the junction of the cervix in the body and should have included the so-called Mackenrodt ligament. Other sections were then taken lateral to this one at distances of ½ cm. transversely across the uterine artery and all its surrounding cellular and fibrous tissue, so that any ligament running from the uterus toward the lateral pelvic wall would be caught and transsected by these sections. Similar sections were also

taken from operating room material after operations of complete hysterectomy. All of these sections were stained by the Van Gieson differential method (by means of which fibrous and muscle tissue are easily distinguished).

In the section of the rectovaginal septum, beginning at the upper end and running down to the perineum, the vaginal wall is separated from the rectum only by loose areolar connective tissue. Nowhere in this septum was there any fascial tissue.

In the section through the vesicovaginal septum in the median line, the wall of the bladder is separated from the cervix and vagina by a loose areolar connective tissue in which nerve bundles and blood vessels can be seen, but there is no evidence of any fascia. Since these findings offer nothing new but are merely confirmatory of Goff's results no illustrations are presented.

Fig. 1 shows the tissue in a longitudinal section of the left side of the uterine artery as it courses along the uterus. Here can be seen the cellular and fibrous tissue along the junction of the cervix and body, a longitudinal portion of the uterine vein and a cross-section of the uterine artery just as it turns up to course along side of the uterus.

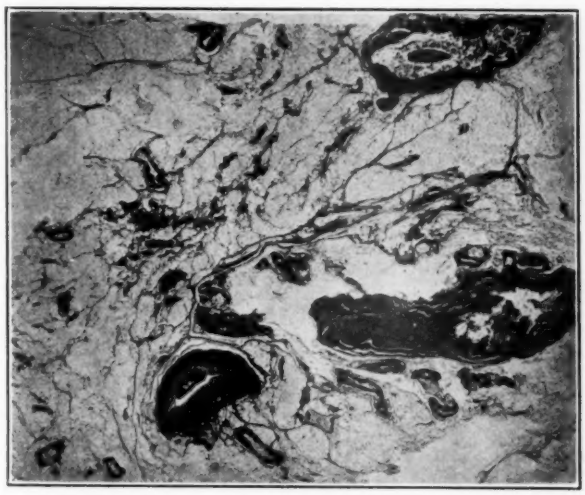

Fig. 3.—Ureter, uterine artery and vein in cross-sections embedded in loose areolar tissue.

These vessels are surrounded by a loose areolar connective tissue with no sign of a distinct fascial or ligamentous structure.

Fig. 2 taken from a section 1 cm. lateral to the previous figure shows a cross-section of the uterine artery, a longitudinal section of the uterine vein and a cross-section of two of its larger tributaries and also a cross-section of the ureter all surrounded by loose areolar connective tissue with no fascia or ligamentous tissue.

Fig. 3 shows the section taken ½ cm. further lateral with the ureter, artery, and vein in cross-section. All are completely imbedded in loose areolar tissue. Near the artery is a vein partially closed with calcareous deposit around which a layer of muscle and fibrous tissue which is a tangential section. There is no sign of any ligament.

Fig. 4 shows a transverse section through the parametrium just above the vagina and lateral to the uterus. In the center is the ureter; on one side is the vein and on the other side is the artery cut across twice because of tortuosity. At one side of the section is a wall of the broad ligament. There is considerable loose areolar connective tissue and fat tissue all around the vessels but no ligament or fascial structure.

Fig. 3 is a section of the broad ligament taken parallel to the lateral wall of the uterus. It shows the vessels of the tube at one end, the round ligament near the middle and the uterine vessels at the other end, with considerable fat tissue but no sign of fascial structure or ligament.

Examination of cross sections of parametrium adjoining the junction of the uterine body and cervix through which coursed the uterine vessels taken from operative material obtained from cases where total hysterectomy was performed corroborated the findings in the autopsy material. Nowhere in the tissue around the uterine vessels as they approached or reached the uterus, was any ligamentous tissue found.

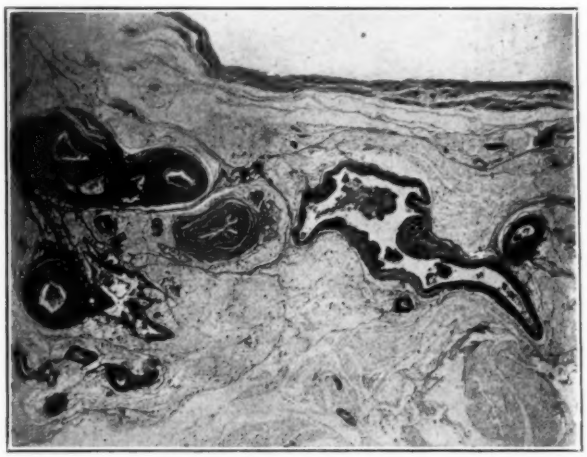

Fig. 4.—Further lateral with ureter and vessels but no uteropelvic ligament.

Fig. 5.—Section of broad ligament parallel to the lateral wall of the uterus showing the round ligament and uterine vessels but no fascial structure or ligament.

COMMENT

Microscopically, there is no well formed, dense, fascial tissue in either the rectovaginal or vesicovaginal septum. The tissue separating the rectal from the vaginal, and the vesical from the vaginal walls is a loose, areolar connective tissue. The tissue, because of its character and composition, could have no restraining action in the prevention of either rectocele or cystocele and could also have no value in the repair of such conditions.

Macroscopically, in the adult, there is no tissue found in the neighborhood of the uterine artery extending from the uterus at the junction of

the cervix in the body outward toward the lateral wall of the pelvis, which is at all comparable to the ligamentous structure known as the cardinal ligament.

Microscopically, in the adult, there is no such tissue demonstrable. That the round ligament could not be the only mechanism by means of which the uterus was kept in its normal position is certainly generally accepted by now. Were there a similar ligamentous structure attached to the uterus at the junction of the body and cervix and to the lateral pelvic wall it would still remain to be shown that it was the only or even an important factor in the maintenance of the normal position of the uterus. According to our histologic studies however, no such tissue is available for the support of the uterus, either as a distinct ligament or distinct fascia. The only tissues found in that neighborhood were loose areolar connective tissue and fat. Thus, the prominence given to the uteropelvic or infundibulopelvic or Mackenrodt ligaments as supports of the uterus is unwarranted. Not only is there no such ligamentous tissue but the prominence given to these ligaments as supporting structures to the uterus, is totally unwarranted. It is interesting to note in this connection that in Piersol's and Gray's anatomy, under the heading of uterine support, mention is made only of the round, broad, and uterosacral ligaments.

It also becomes manifest then that the operations for the cure of prolapse by plication or shortening of the cardinal or Mackenrodt ligament as advocated by Nyulasy[5] have no rational basis.

Also in proposing a rational explanation for the development of prolapse, and its cure, these so-called ligaments must be excluded from consideration.

CONCLUSION

There is no ligamentous tissue, which might by its presence be able to support the uterus, to be found in the base of the broad ligament around or near the uterine vessels and extending from the uterus out to the lateral pelvic wall as described in some texts under the name of Mackenrodt ligament, the cardinal ligament, the uteropelvic ligament or the infundibulopelvic ligament. The name ligament attached to any structure existing in the base of the broad ligament and surrounding or near the uterine vessels, extending from the cervix out to the lateral pelvic wall is a misnomer and is distinctly misleading. The uterus cannot depend for support on any structure to be found in the base of the broad ligament, running from the cervix out to the lateral pelvic wall and previously designated as the Mackenrodt, the cardinal, the uteropelvic or the infundibulopelvic ligament any more than it can on any and all the tissues to which it is attached. The explanation of the development of prolapse and its cure, can no longer include a consideration of these so-called ligaments. Operations designed for the cure of prolapse of the uterus by shortening the so-called cardinal, Mackenrodt, uteropelvic or infundibulopelvic ligaments have no rational basis.

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284 New York Avenue.

INTERNAL ROTATION OF THE FETAL HEAD FROM THE VIEWPOINT OF COMPARATIVE OBSTETRICS*

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THE scientific investigation of the mechanism of labor began with Ould in 1742[1] when he observed that the fetal head entered the pelvic excavation with the sagittal suture in the transverse diameter. The prevailing theory at that time was that the fetal head entered and passed through the pelvic excavation with the sagittal suture in the anteroposterior diameter, appearing as if the child crept into the world. Saxtorph[2] and Solaryes[3] threw more light on this question by their observation that the fetal head entered the pelvic excavation with the sagittal suture in one of the oblique diameters, a view supported by Baudeloeque[4] and Naegele[5] and now generally accepted by the profession. Levret[6] in 1762 emphasized the importance of the mechanical factor in labor thus giving rise to the so-called obstetrico-mathematical school which was to influence later obstetric thought. Rigby[7] in 1841, realizing the mechanical trend of obstetric thought, wrote, "In the last century, it was so the fashion to resolve every physiologic process into a mathematical problem." Our studies of the physiology of the uterus in labor[8, 9] have caused us to inquire into the mechanism of the internal anterior rotation of the fetal head. These studies have led us to the conclusion that the uterus plays an important rôle in rotating the fetus, particularly in lower animals.

A review of the literature will demonstrate that internal rotation of the fetal head appears to be based, in the main, upon the mechanical factors of the pelvis. On the contrary, a number of writers have presented evidence that the uterus, or even the fetus, is or may be a factor. No attempt will be made at this time to review the evidence *pro* and *con* and to discuss the various theories. However, having made such a review, we are of the opinion that the teaching of Denman[10] and Rigby,[7] which maintains that the adaptation to and propulsion of the fetus through the pelvic cavity is only a mechanical incident resulting from a physiologic process, has not been sufficiently appreciated.

*Read at a meeting of the Chicago Gynecological Society, February 19, 1932.

It occurred to us that a study of comparative obstetrics or the phylogenetic history of pregnancy and parturition might throw some light on the subject. We shall briefly outline the evolution of the pelvis, the physiology of the uterus in labor in vertebrates, and record the observations we have made on internal rotation of the fetus in the parturient dog, pointing out that due to morphologic changes in the pelvis, the uterus accommodates its function accordingly.

THE PELVIS

In the following brief review of the comparative anatomy of the pelvis,[11 to 23] it will be noted that as the progenitors of man became more erect, the architecture of the pelvis changed to meet the requirements best suited to subserve the function required by the orthograde posture.

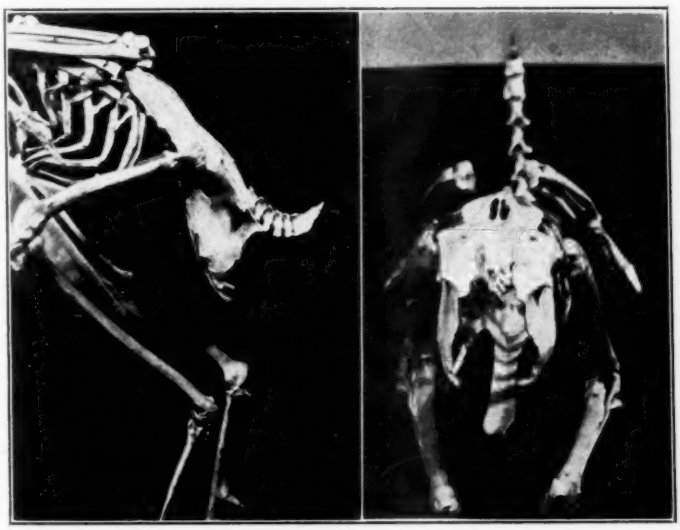

Fig. 1.—Photograph of the lateral and posterior views of the pelvis of the chicken.

In the fish, the primary requirement for existence is locomotion, so that Nature has provided the spinal column for that purpose. The caudal vertebrae are particularly mobile and not hampered by a definite pelvic girdle to hinder the mechanism of propulsion. Here we find the first rudimentary indication of a pelvis consisting of two calcified or evenly ossified pelvic plates which become segmented from the basal cartilage and are held in place by either a cartilaginous or a ligamentous attachment.

In birds, we come to a group whose existence is dependent both on flight and on the ability to use the hind limbs for locomotion on land. The exception to the rule is presented by the South African ostrich which has a well formed pelvis and depends on its hind limbs for locomotion in flight. The vertebral column is semirigid and the pelvis is designed to support the hind limbs. The pelvis is developed more dorsally than ventrally. It is fixed posteriorly to the lateral part of the sacrum. Anteriorly the two halves of the pelvis are separated from each other, but are connected by either a cartilaginous or ligamentous attachment, which completes the pelvic girdle (Fig. 1). In fish and in birds, the pelvic aperture is large in comparison to the eggs that must pass through, so that in the expulsion they do not meet with much mechanical resistance.

The pelvis of the mammal is firmly attached to the vertebral column and there exists a union of the pubes and ischium anteriorly in the midline to form a symphysis. By gradual stages, the ischium spreads laterally from the ischiopubic symphysis, forming the pelvic arch, which is clearly demonstrated by a study of the dry pelvis of the mammal (Fig. 2).

A study of the pelvis of the monotremes, marsupials, rodents, ungulates, carnivores, and the monkeys demonstrates that the symphysis is quite long, and that the ischiopubic arch varies.

In the anthropoid apes and in man, we note a radical change from the lower mammals in that the ischiopubic symphysis changes. The symphysis becomes shorter and the pubic arch greater, reaching its greatest relative shortness and forming the greatest pelvic arch in man (Fig. 2). Schumann[17] points out that in the lower animals the ischiopubic symphysis is approximately one-half of the pelvic length. The infantile human pelvis is like that of a quadruped pelvis in that its anteroposterior diameter is greater than the transverse and is quite similar to that of the highest apes. This change in the morphology and length of the symphysis is related to the evolution in the mode of the mechanism of labor of all vertebratae in that the diameters of the pelvic inlet in relation to the fully developed fetus play a rôle in determining the position of the presenting part for physiologic birth. For a complete review, the reader is referred to Schumann.[18]

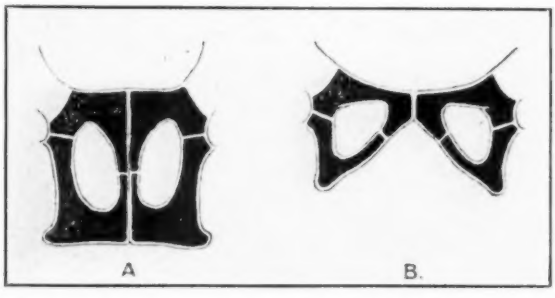

Fig. 2.—Diagrammatic representations of (A) the primitive mammalian and (B) the human type of ventral symphysis. (Taken from Jones, *Arboreal Man.*)

PARTURITION

In fish, most of which are oviparous, the ova are stored in an ovisac which is part of the celomic cavity. Spawning is brought about by abdominal contractions and the unfertilized ova pass out through the abdominal pores. The shark-like fish (Elasmobranchii)[24, 25] are ovoviviparous and oviparous. The eggs are fertilized in the oviducts and develop in the uterine enlargements of the ducts. In the shark-like fish which are viviparous, we must assume that the fetus or fetuses at term are expelled from the uterus by a mechanism of parturition consisting of a relaxation of the genital openings, and of abdominal and uterine contractions.

In birds which are oviparous, we find that the anatomy and the physiology of parturition are closely allied to the higher mammals. Verrier[26] in 1884 compared the normal parturition in the human being to the rotation of the egg within the oviduct of oviparous (birds) animals before its exit. The müllerian ducts, one on each side of the vertebral column, form the oviducts. At maturity, the right oviduct and ovary atrophy. After the ripening of the yolk, it enters the ostium abdominale tubae of the left oviduct, passing down through the oviduct in a spiral rotatory manner on its chalazal axis due to peristaltic activity. The musculature of the oviduct is spirally arranged. During the descent of the egg, the albuminous layer is deposited in spiral coats. The shell membrane is laid on in the uterus.

The egg passes down the oviduct with the pointed end first.[27 to 32] Aristotle[34] wrote that the blunt end of the egg is laid first. This has been confirmed.[35 to 38] Due to the work of Wickman,[31] it appears to be settled that the egg passes down the oviduct with the pointed end first, but that in the expulsion of the egg from the shell-gland or uterus, it is turned usually 180 degrees on its short axis to be deposited externally with the blunt end first. That is, the egg undergoes a "version of 180 degrees" usually before or during the delivery of the egg.

The mechanism of the delivery of the egg: From the uterus or shell-gland the egg is emptied into the cloaca by the relaxation of a strong sphincter at the lower pole of the uterus and peristalsis of the uterus. The expulsion of the egg from the cloaca is accomplished by a mechanism of eversion of the cloaca, or, the uterus still enveloping the egg is prolapsed through the cloaca and the vagina and the egg is laid without having touched the walls of either the cloaca or the vagina.[33]

The pelvis is very probably a mechanical hindrance to the physiologic function of the uterus and is not essential for parturition in certain lower forms. This is indicated by a study of the shark-like fish (Elasmobranchii), the whale (cetacea),[39 to 43] and the seal, sea lion and walrus (aquatic carnivora) which have only a rudimentary pelvis and are viviparous. In the shark-like fish, labor must be dependent upon the uterine and abdominal contractions. In the whale and in the seal, sea lion and walrus, the uterus is bicornate, so the mechanism of labor should be the same theoretically as occurs in those terrestrial animals which have a uterus bicornis. Since they have only a rudimentary pelvis, the pelvis is not essential for parturition in these animals which possess a uterus intermediate in differentiation.

In the monotremes, the two müllerian ducts become the two uteri. Each opens into the urogenital sinus on its respective side. These animals are egg-laying mammals, and we may assume that the mechanism of egg-laying is similar to the birds. How they are propelled through the urogenital sinus and the cloaca, we have been unable to determine.

In the marsupials, the two müllerian ducts become the two uteri which fuse just before reaching the urogenital sinus. The fused portion becomes the vagina, which opens almost immediately into the cloaca. These animals are egg-laying mammals and we assume that the fertilized ovum is propelled downwards through the uterus and through the cloaca to the vulva in the same manner as in the bird. Parturition takes place with the fetus in a premature state in the egg, which is arrested at the vulva, where the shell membrane ruptures. The fetus reaches the marsupia by its own locomotion and becomes fixed to a teat of the mammary gland.[44]

From the rodents to man, we reach a stage in the evolution of the uterus and parturition on the basis of which we may correlate homology and physiology.

In the uterus didelphys, uterus bicornis and the uterus simplex, we find certain outstanding structural and functional analogies as follows: The upper uterine segment which has the property of isometric contraction and retraction, manifests powerful peristaltoid contractions. The lower uterine segment with its property of relaxing, stretching or thinning manifests "less powerful" peristaltoid contractions. In addition, we find the presence of the "Ring of Bandl" (fundal sphincters) between the upper (cornua) and the lower (corpus uteri) uterine segments, and its correlated physiologic properties; the cervix uteri with its cervical canal, os internum and os externum and the similarity of its functions, being plugged during the pregnant state by mucus; and that during the second stage of labor, the uterus is assisted in the expulsion of the contained ovoid by the auxiliary forces.

In the rodents, the uteri are perfectly formed, each with a well-formed cervix, separated from each other, but opening into a single vagina (uterus didelphys). During labor, one of the lowermost ampullae of one uterus becomes active, divides into an upper and a lower uterine segment, and manifests a mechanism of labor that is similar to other mammals. The fetuses are expelled normally in a dorsosacral position. The lower

uterine segment is derived from the lowermost ampulla of each uterus and is the common lower uterine segment for the expulsion of each successive fetus from each respective uterus.[45] The upper uterine segment is derived from the upper part of the lowermost ampulla by retraction and a sustained longitudinal contraction. After the expulsion of the first fetus that part of the upper uterine segment merges with the ampullae above by retraction, and becomes in part the upper uterine segment for the mechanism of expulsion of each successive fetus from that uterus. This merging of the ampullae goes on until all of the fetuses are expelled. This physiology of the uterus of the rodent (rabbit) in labor will be published in more detail in a future publication.

In the carnivores, we have the formation of the uterus bicornis unicollis. The two müllerian ducts fuse into a single tube at the lower or caudal extremities to become the corpus uteri or the lower uterine segment, with one cervix opening into a single vagina; the upper or the cephalic extremities remain separated to form the cornua or horns, which are quite long. We have studied the physiology of labor in the dog,[8] and we will briefly review the first and second stages of labor. The first stage is the expulsion of the lowermost fetus from one of the lowermost ampullae. The corresponding fundal sphincter (Ring of Bandl) relaxes, and by retraction of the musculature of that ampulla the fetus is expelled into the corpus uteri. The second stage begins with a fetus in the corpus uteri when the relaxed fundal sphincter contracts, while the other sphincter holds it tone; and contractions of the corpus uteri aided by the auxiliary forces bring about the expulsion of the fetus. The mechanism of the cervix is probably the same as in the human being, but whether the dilatation occurs during the expulsion of the fetus from the cornu or after the fetus has entered the corpus uteri is as yet not known.

In the ungulates, the same anatomical arrangement is found as in the carnivores, except that the cornua or horns are relatively much shorter and the cervix is much more developed. During pregnancy, the fetus or fetuses are developed in the cornu, or cornua in the case of twins, and the corpus uteri. We have studied the physiology of the uterus in the sheep in labor, and in pregnant uteri of the cow in various stages during pregnancy. With the onset of labor, the pregnant cornu with each uterine contraction shortens by its property of retraction and pulls upward on the fundal sphincter. The continued shortening of the cornu or the upper uterine segment has the effect on the corpus uteri or the lower uterine segment of stretching or thinning it. This we believe brings about some cervical effacement and dilatation, which is further amplified by the presenting portion of the fetus in the corpus uteri. With the dilatation completed, the contraction of the cornu brings about expulsion of the fetus aided by the auxiliary forces.

In the primates, we find a complete fusion of the upper and the lower portions of the müllerian ducts forming a uterus simplex or arcuatus with a cervix which opens into a single vagina. Ivy, Hartman and Koff[46] have studied the physiology of the uterus in labor in the macacus rhesus and have pointed out certain homologies and analogies between the uterus of the monkey, dog, and man. It is known and can be demonstrated that the fetal head enters the pelvic cavity with the head in complete extension, the fetus being delivered in a position similar to the rodent, dog and mare, that is, in a dorsosacral position. A study of the monkey's pelvis demonstrates its similarity to that of the carnivores and ungulates, except that the promontory of the sacrum is more marked in the monkey. A study of the fetal skull and maternal pelvis in the monkey shows that the head must pass through the pelvic cavity in extension in a dorsosacral position. During pregnancy, Hartman[47] has found that the back of the monkey fetus is to the right or left side of the mother's abdomen.

In the anthropoid apes, the literature of the mechanism of labor is very meager. Fox[48] has described labor in a chimpanzee with the head delivering as an occipitoposterior. After the delivery, the face rotated to the left. Tinklepaugh[49] described a portion

of parturition in a chimpanzee (during labor the chimpanzee became frightened and jumped onto a screen partition, and in the jump the fetus was expelled). Five days before the delivery, the position of the fetus was O.L.A. Just before the animal jumped, the head appeared at the vulva with the sagittal suture in the anteroposterior diameter, and the occiput posterior. From a comparative study of the dry pelvis and the skull of the anthropoid apes, it would appear that the fetal head should be delivered as in the human being, through the pelvic cavity by internal anterior rotation, because the transverse diameter is greater than the anteroposterior diameter of the pelvic inlet.

INTERNAL ROTATION

The position of the fetus in utero during pregnancy and labor in the ungulates will be presented in order to emphasize the type of internal rotation that occurs. We will study the mare (Ruminantia).[50 to 55]

During pregnancy, the fetus or foal lies usually in one of the cornua and the corpus uteri on its back on the floor of the mare's abdomen with the head towards the pelvic inlet and the hind end in the upper end of the gravid horn. The fetal chin is on the chest, the fore legs bent at the knee, and the hind legs flexed. This is the dorsopubic position (Fig. 3). The foal may lie on its side or in the dorsoiliac position (Fig. 4). Williams[50] has recently found that the dorsopubic position is not the only prenatal position of the foal, since he and his associates have found by rectal palpation that the foal may lie either in a dorsoiliac or a dorsosacral position. A roentgen study has not been made. The presentation is anterior or cephalic in from 95 to 96 per cent.[50]

A study of the pelvis and the fetal head of the mare, cow, and sheep demonstrates that the physiologic relations between the diameters of the pelvis and the presenting part of the fetus are such that in the mechanism of labor the fetus must rotate frequently from 90 to 180 degrees, or from the dorsoiliac or the dorsopubic position, in order to reach the normal presentation and position of a cephalic dorsosacral position for physiologic birth (Fig. 5). In a hind end or breech presentation and position, the foal must be with the back to the maternal back with the hind legs fully extended which is a posterior or breech dorsosacral position. This rotation occurs preparatory to birth or during the first stage of labor. The presentation undergoes changes in which the fore legs and head are extended; the vertex is in relation to the hollow of the sacrum, and the chin and the anterior portion of the neck are in relation to the ischiopubic symphysis. As the head is being delivered, restitution begins to occur, which is flexion of the head or a return to the position in which the head was prior to labor. It is to be noted that when effacement and dilatation of the cervix are completed, and the foal is in position for delivery, it must ascend about 45 degrees in order to pass over the ischiopubic symphysis and through the pelvic inlet.

We may add, at this time, that the component parts of the mare's uterus may be compared to the human uterus at this stage. The pregnant cornu is analogous to the upper uterine segment. The corpus uteri and the cervix are analogous to the lower uterine segment and the cervix. At the junction of the cornua and the corpus uteri is found a definite sphincter-like structure which we call the fundal sphincter, similarly to the structure found in the dog,[5] which is analogous, we believe, to the "Ring of Bandl." During labor, the nonpregnant cornu, which has also undergone hypertrophy, is kept closed by an isometric contraction of its corresponding fundal sphincter which prevents the foal from entering the nonpregnant cornu. The veterinarian literature states that the nongravid horn is kept closed and prevents the foal from entering on account of a synchronous contraction with the active gravid cornu; (we believe that the nongravid horn is to be considered more or less passive during parturition).

With the foal in a normal presentation and position, the expulsion of the animal is brought about by the uterine activity of three types: (a) contraction, (b) "isometric

shortening'' of the longitudinal muscles with retraction of the horn, and (c) stretching and relaxation of the corpus uteri with effacement and dilatation of the cervix. The horn thickens or ''caps'' due to the isometric contraction or the sustained contraction of the longitudinal musculature. The corpus uteri by relaxing and being

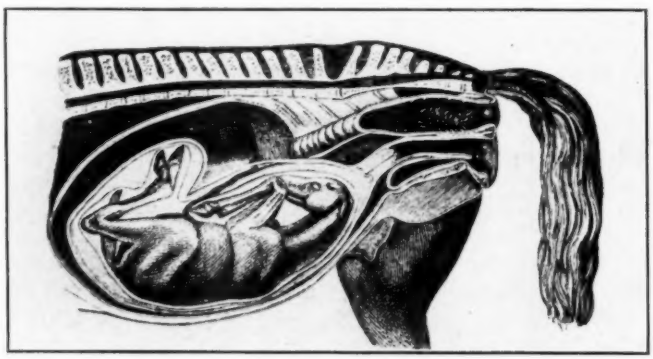

Fig. 3.—Shows the position of the foal in utero near term. (Taken from Franck, Handbuch der Tierärztlichen Medizin, revised by Albrecht.)

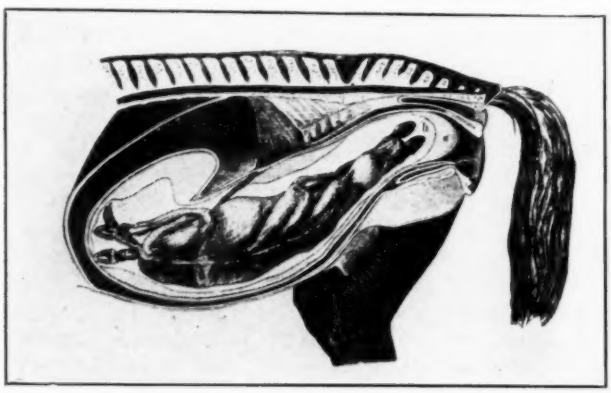

Fig. 4.—Shows the position of the foal early in labor in the dorsoiliac position, partial rotation. (Taken from Franck, Handbuch der Tierärztlichen Medizin, revised by Albrecht.)

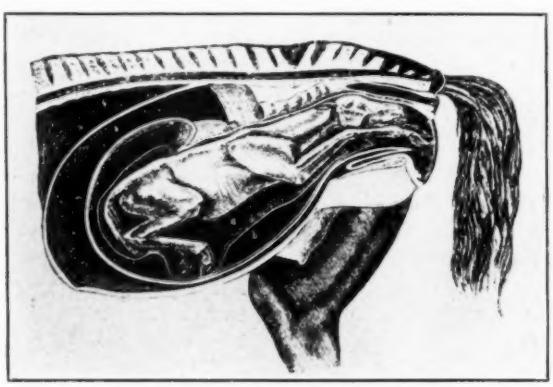

Fig. 5.—Shows the position of the foal in labor rotated to the dorsosacral position for physiologic birth. (Taken from Franck, Handbuch der Tierärztlichen Medizin, revised by Albrecht.)

stretched bring about effacement and dilatation of the cervix along with relaxation of the smooth muscle forming the cervical sphincter.

A consideration of the anatomy of the pelvis and the uterus in the mare, and the changes of the foal on its longitudinal axis excites the query, what causes the rotation of the foal? Smith[54] and de Bruin[52] state that the uterine contractions cause the foal to be rotated on its longitudinal axis; and that the extension of the fore legs is due to

Fig. 6.—A.—A roentgenogram of a dog in labor. The head is entering the corpus uteri in a cephalic dorsopubic position. The body is approximately in a dorsoiliac position.

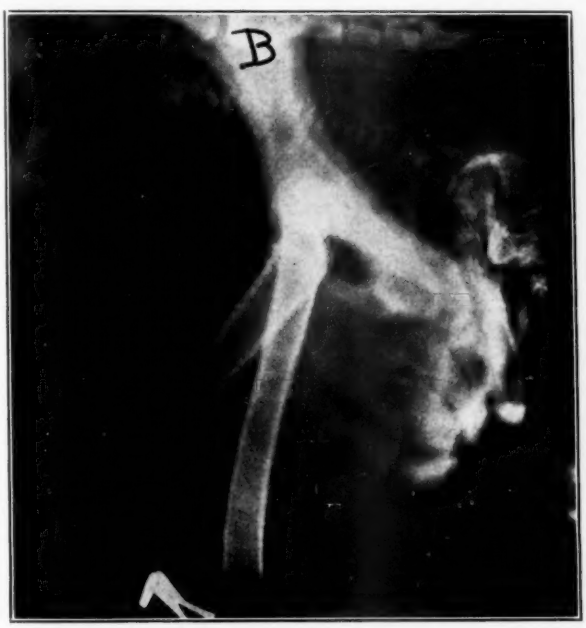

Fig. 6.—B.—A roentgenogram of the same dog as in Fig. 6-A with the head and body rotated to a dorsosacral position, the head being at the outlet. Similar rotation may occur before the head passes the inlet.

the result of the fetal movements. The gravid horn is so placed that the angle between the axis of the gravid horn and pelvic axis is about 45 degrees. The resistance that the presenting part meets occurs only during the duration of the uterine contractions. In the interval between the uterine contractions, we can readily see that by gravity and relaxation of the uterus the foal would tend to lose its contact with the bony pelvic inlet. Recalling the above outlined changes of the position of the foal, we note that the inclined planes, the ischial spines, and the pelvic floor of the mare take no part in aiding or bringing about internal rotation of the foal on its longitudinal axis. Since the pelvic inlet cannot account for the rotation, and since we cannot believe that the fetus crawls into position, we must accept the premise that the uterine contractions are responsible for the rotation of the foal into a normal presentation and position for the physiologic birth.

Because of the similarity of the pelvis and the uterus between the ungulates and the carnivores, we undertook a roentgenographic study in the dog to determine the position of the fetuses during pregnancy and parturition.

Roentgenograms of pregnant dogs from thirty days to near term were made. On the onset of labor or after one or more pups had been delivered, roentgenograms were taken at intervals, or in series. By direct observation, we have also determined under anesthesia with the abdomen open, the presentation and position in which the pups were delivered. A majority of the deliveries were studied by vaginal examinations during the passage of the pups through the pelvic cavity, the findings being correlated with the x-ray plates. No anesthesia was required. All dogs cooperated remarkably well. The roentgenograms were taken in three positions: lateral with the dog lying on the plate; lateral with the dog standing on all fours with the plate held in position by a specially constructed, adjustable plate holder; on its back with the fore and hind legs held apart on a plate. We found that the most practical position was with the dog lying on its side. Roentgenograms show that this position does not cause a material change in the position of the fetuses. Fourteen dogs were studied during pregnancy and labor.

During pregnancy, the roentgenograms showed that the majority of the pups in the horns are in a dorsopubic position, with some in a dorsosacral position, and others in a transverse position. The transverse position is due to the marked enlargement of the horns which become somewhat flexed on themselves, so that an "apparent" transverse position is found on the roentgenogram.

NOTE: For lack of space the protocols of the experiments made in dogs cannot be included.

Our evidence shows that the presenting fetus not only rotates during its passage through the corpus uteri, but may rotate (but not always) to a dorsosacral position before it enters the pelvic inlet. Every one of the ninety pups whose birth was observed was delivered in a dorsosacral position. If the fetus enters the corpus uteri in an approximate dorsosacral position, very little rotation may result. "Superrotation" occurred in one instance. The fetus may enter the pelvic inlet in a dorsoiliac or dorsopubic position, but in such instances, rotation to a dorsosacral position occurred before birth.

The rotation to a dorsosacral position is practically complete as a rule before the fetus strikes the pelvic floor. The head is fully extended during passage through the corpus uteri. We could not decide from our

roentgenograms the direction of the rotation, or whether the direction depended on the horn from which the fetus passed. This is an important point because the direction of rotation may depend on the horn from which the fetus comes and which is turn may have some bearing on the direction of rotation of the fetal body in the human being.

The long labors were apparently due to abnormal positions caused by uterine dysfunction. It is interesting that one fetus may be delivered slowly and apparently with difficulty, and then the following fetus be delivered within a few minutes. This indicates that the disturbed function was temporary. The observed fact is that in the dog the fetus rotates during passage through the corpus uteri.

SUMMARIZING STUDY OF COMPARATIVE OBSTETRICS

A review of our knowledge of comparative obstetrics emphasizes the exceedingly interesting evolution of the morphology of the pelvis and the uterus and throws light on the physiology of the uterus. The gradual change of the pelvis from the fish to the human being demonstrates the relation of structure to functional activity. The change in the postural attitude from the pronograde to the orthograde was associated with a logical mechanical change in the architecture of the pelvic girdle.

The oviduct of the bird propels the yolk downward in a spiral manner to the shell gland or uterus, and "version" of the egg of 180 degrees on its short axis occurs[33] usually in its delivery. In the mare, the foal is rotated frequently from 90 to 180 degrees for physiologic birth in a dorsosacral position or in the largest pelvic diameter. We have found in the dog that the fetus is rotated in some instances from 90 to 180 degrees for physiologic birth. This amount of rotation may or may not occur (usually does not) before the fetus enters the pelvic inlet, the amount of rotation varying with the position in which the fetus enters the corpus uteri. Most of the rotation occurs in the corpus uteri or just before the fetus enters the vagina. In this connection it is interesting that rupture of the uterus has been observed[56] in the dog due to impaction of the forepart of the fetus in the pelvic cavity in a dorsopubic position, which is analogous to impaction in the mentoposterior position in the human being. Hartman's[57] study of parturition in the monkey (Macacus rhesus) has demonstrated that the fetus is delivered in a dorsosacral position with the head fully extended. It was found[47] by palpation that the back of the monkey fetus is found usually to the right or left side of the mother's abdomen. Our study of the monkey's pelvis has shown its similarity to the pelvis of the dog and mare in regard to the pelvic inlet and cavity, except that in the monkey, the promontory of the sacrum is more marked. And a study of the fetal skull and maternal pelvis shows that the only manner in which the head could pass through the pelvic cavity without meeting considerable obstruction or even impaction resulting, is in extension in a dorsosacral position, the body following through. On the basis

of our studies, we must conclude that in lower animals the uterus is primarily responsible for placing the fetus in a dorsosacral position with head extended, the position in which is found the greatest pelvic diameter, for physiologic birth. The truth of this generalization was recognized by Schumann, who in speaking of rotation points out that it consists "not in rotation of the presenting part upon the pelvic floor, nor do the pelvic walls play an important rôle in this phenomenon," it being more of an accommodation of the greatest diameter of the fetus to the greater axis of the maternal pelvis.

CHIEF DIFFERENCE BETWEEN LOWER FORMS AND THE HUMAN BEING

In the apes, monkeys, and quadrupeds, the largest pelvic diameter throughout is anteroposterior, whereas in the adult human being at the inlet the largest diameter is transverse, the promontory of the sacrum being more marked. In these lower forms, the fetal head is delivered in extension, occipitoposterior (not definitely settled in apes), in the human being, occipitoanterior. In these animals and in the human being, the head is born in the anteroposterior, or largest diameter of the outlet, but with opposite positions of the occiput. In other words, the change in the diameter of the pelvic inlet has been associated with a change in the position of delivery of the occiput. This is a fundamental difference, since even in most occipitoposterior positions in the human being, anterior rotation occurs.

Another outstanding difference is in the position of the head during passage through the pelvis. In these lower forms, the head is in extension throughout, flexion occuring only after the chin has passed the ischiopubic symphysis. In the dog the head is extended during passage through the corpus uteri. In the human being, the opposite occurs; the head enters the pelvis slightly flexed, then flexion becomes very marked, deflexion occurring as the occiput passes the symphysis. The mechanism of delivery of a human fetus in a mentoanterior position is quite analogous to that of the dog.

Further difference is found in the curvature of the birth canal. In these lower forms, although the birth canal is curved anteriorly, it is less so than in the human being.

We maintain, on the basis of our observations, that there is no difference in regard to the snugness with which the fetus fits into the birth canal. However, a difference does exist in regard to the amount of obstruction met with at the level of the pelvic floor. In lower animals the fetus is usually rotated into the position of least resistance before it strikes the pelvic floor; whereas, in the human being this is not entirely true, since the pelvic floor does play some rôle in rotation.

Since the uterus of lower animals is apparently the chief factor which accommodates the fetus to the pelvic cavity for physiologic birth, the

questions arise, has the human uterus retained this phylogenetic property of rotating and adapting the fetal ovoid in relation to the morphologically changed pelvis, or as the morphology of the pelvis changed, did the fundamental physiology of the uterus change?

COMMENT

In the Human Being.—It is known that all hollow viscera have a normal shape and posture which are maintained primarily by the anatomical arrangement and tone of the muscle fibers. Changes in tone of the muscle fibers lead to changes in postural tone (length and tension of muscle fiber) of the organ, or the outline, contour and position of the contents of the viscus. Gravity affects the posture of a muscular viscus, particularly if the abdominal musculature is atonic; but obviously this means that the tone of the muscle of the viscus is insufficient to overcome the influence of gravity (ligamentous supports remaining constant). These facts are pointed out to indicate that the postural tone of the uterus is an important factor in determining the position of the fetus during the latter part of pregnancy and more particularly during labor except in cases of polyhydramnion. In cases of polyhydramnion that come to term, and in multiparae with a flaccid uterus and lax abdominal walls, it is known that malpresentations frequently occur.[58] In a previous article[9] we have presented evidence indicating that the uterus possesses a coordinating mechanism, which makes possible a purposeful and harmonious movement, a disturbance of which causes variations in muscular tone in different portions and may lead to abnormal positions, presentations, or prolonged labor. We maintain, therefore, that the postural tone of the uterine musculature which is, of course, markedly increased during contractions, is the basic factor concerned in determining the presentation and position. This is somewhat analogous to the view of Olshausen,[59] Schmitt,[60] which was accepted by Bumm[61] and others[62 to 66] which holds that in labor, "the uterus tends to assume its original flattened form," and is analogus to the "theory of accommodation," which with gravity, is used to explain the frequency of cephalic presentation.

Our contention is that as the transverse diameter of the human pelvis became the larger diameter, the uterus adapted its physiology to meet this change in morphology. It is difficult for us to believe that the fact that the sagittal suture enters most commonly either the oblique or transverse diameter of the pelvic inlet in man is a "mechanical accident," or that "Nature," in such an important process as birth, would rely solely on the possibility that force applied to the fetal ovoid would cause it to seek the larger opening, or that the "directing force" manifested by the uterus in lower animals has been lost entirely by the human uterus. However, we do not intend to imply that mechanical factors do not play a rôle in the causation of flexion, deflexion, and rotation.*

*It is not within the province of this paper to consider cephalopelvic disproportion.

In the dog, we have observed abnormal positions at the inlet. Although associated with prolonged labor, the abnormal position may be corrected in time by the uterus, or before the head has passed through the cervix, or much beyond the inlet. Analogously in the human being it is not uncommon to find the head in an abnormal presentation at term (x-ray), i. e., a brow, a mento or an intermediate presentation, and in the majority of cases the malpresentation is corrected spontaneously. Also in most cases of "deflexion attitude," spontaneous correction occurs. The question arises, is the uterus, or the mechanics of the pelvis, primarily concerned in the production and correction of such conditions?

In a previous paper we have expressed our conclusions in regard to malpresentations.[9]

In regard to deflexion attitudes, obstetric experience teaches that such a condition is associated with a dystocia syndrome characterized by prolonged labor, slow effacement and dilatation, lack of descent of the head, arrest, or slow rotation of the fetal head, and so-called inertia uteri. (We believe that inertia uteri is a condition in which the longitudinal and oblique muscles fibers of the upper segment do not manifest their important property in labor of isometric contraction, or sustained longitudinal shortening, which leads to retraction and "capping" and holds or fixes the progress or advantage gained by the preceding contractions.) The attitude of the head in the dog in labor is controlled by the same factors that operate in the human being, namely, a harmoniously contracting uterus throughout, the resistance to egress, and the classical unequally balanced two-armed lever than exists between the vertebral column (the support) and the head (a long and a short arm) (see Williams[69]). In order to get flexion of the head in the canine fetus, the snout would have to be lodged in a "paralyzed" pocket in the corpus uteri or caught in a pocket proximal to a bony protuberance. In cases of normal cephalopelvic relations in the human being, the uterus must be viewed as the primary cause of flexion because the force of the uterus, contracting uniformly in its various portions, is transmitted to the fetal spinal column. If the force transmitted through the fetal spinal column is misdirected by improper coordination of the upper uterine segment, or if the lower segment or cervix is more atonic or yielding in one portion than another, the lever action will be modified or abnormal. This may or may not be corrected by a resumption of normal uterine activity without which even the normally distributed resistances in the pelvic canal would be of no avail. This property of the uterus has been referred to by Solaryes[68] as the "reflected force" and by Winchell[69] as the "guiding line." Of course it is to be recognized that structural abnormalities in the pelvis, tumors, etc., may be the primary cause of deflexion.

That internal rotation is not a simple phenomenon is shown, first, by the large number of explanations that have been offered, and second, by

the fact that the head may be rotated either right or left depending on the position, and that during delivery the head may be rotated in one direction and then later the shoulders in the opposite direction. Most of the explanations offered are based entirely on mechanics. Only a few maintain that the uterus plays a primary rôle. Such a difference in opinion generally indicates that no single factor is concerned, as Cragin[70] has pointed out.

Schmitt,[60] Olshausen,[59] Schroeder[71] and Bumm[61] (also Spiegelberg,[72] Barnes,[73] Cazeaux,[74] Gerdy,[75] and others accepted the view in part) have contended that the uterus is the initial factor in rotation of the head because the uterus rotates the trunk anteriorly, the rotation being completed by the gutter-like structure of the pelvic floor. More recently Warnekros[76] after a roentgenographic study of the fetus in labor, reports that the rotation of the body frequently preceded that of the head, but believes the pelvic floor plays the predominant part. That the trunk may exert a rotating effect on the head is shown by the phenomenon of external restitution and by the fact that in a breech delivery, the anterior or posterior rotation of the after-coming head is influenced chiefly by the position of the body (Cragin). The most obvious objection to this view is that it does not explain the rotation of the shoulders that occurs after delivery of the head. In regard to the pelvic floor, we agree with Paramore[77] in that the chief action of the pelvic floor is to project the advancing fetal pole forward in a sagittal plane towards the pelvic arch. This is not rotation. We agree with Edgar[78] in that the advancing fetal pole will tend to move toward the area of least resistance, namely, the vulval slit. On the basis of these views we can conceive and grant that the pelvic floor may rotate the flexed head from a right or left occipitoanterior position (O.L.A. or O.D.A.) or even a transverse position, to an occipitoanterior (O.L.A.) in the second stage of labor. If this is accepted, there is no difficulty in Olshausen's explanation. But we cannot understand how the pelvic floor, the incline planes, ischial spines, Sellheim's theory,[79] etc., per se, may operate in causing anterior rotation of the occiput in posterior positions with full flexion. We believe, therefore, that the rotation of the trunk by the uterus plays an important rôle in rotating anteriorly the occiput in posterior positions and in preventing posterior rotation of the occiput (O.P.)

In this connection, however, the classical experiments of DuBois[80] and Edgar[78] cannot be disregarded. In their experiments, performed on a dead fetus and mother, the fetus (head flexed) was placed in a posterior position and either pushed or pulled through the pelvis. Anterior rotation occurred. This shows unquestionably that the resistance offered by the pelvic walls and floor plays a rôle in the causation of internal anterior rotation. But obviously the force had to be applied to the fetus in a "well directed manner" with the head flexed,[65, 74] since it would cer-

tainly be impossible to express or extract the fetus if the "directing force" were not properly applied to the head. This directing force in life comes from a harmoniously contracting uterus.

We realize that Sellheim's view is more generally accepted. Sellheim's view teaches that a cylindrical body, which can be bent to different degrees in different directions, when forced through a curved cylindrical canal must rotate so that the portion which bends most easily will become accommodated to the curvature of the canal. Since his data on recently delivered babies showed that the head is more readily extended than flexed, he argues that the markedly flexed had tends to extend and and that this tendency will cause the nape of the neck to rotate to the anterior curvature of the birth canal which at the same time causes extension. We cannot accept this explanation for three reasons: first, a dead, unmacerated fetus is rotated in the natural birth process and DuBois and Edgar obtained rotation with a dead fetus experimentally; second, it implies that the lever action of the spinal column on the fetal head operates to cause flexion but not extension of the head, which may be viewed as inconsistent; and third, it holds that rotation is independent of the kind of or directional application of the force applied by the uterus.

The mechanical principles by which the resistance of the pelvic floor and walls operate to facilitate anterior rotation is best explained by Paramore, we believe. Paramore's explanation involves an appreciation of the mechanical principles of the two-armed lever that is concerned in causing flexion and extension. The only difference is that in flexion and extension the resisting force is being applied perpendicularly to a "horizontal" plane and that in rotation the resisting force is being applied perpendicularly to a "vertical" plane. (Of course the planes are not perfectly horizontal or vertical.) With the head well flexed, the forehead is eccentric in that the distance from the fetal axis to the sinciput in the "vertical" plane is greater than the distance from the fetal axis to the occiput. As the vertex strikes the pelvic floor, it is deflected anteriorly The resistance offered to anterior deflection will be more effective on the forehead because the lever arm is longer. Hence, the forehead will move backward about the fetal axis in a screwlike rotatory manner. The levatores ani, decreased resistance of vulval slit and the larger anteroposterior diameter of the outlet will assist after the vertex reaches an anterior position (O.L.A. or O.D.A.). Flexion is essential, since it determines the length of the lever arms or the eccentricity of the forehead. Paramore recognized that an adequate driving force from above was essential to bring the forces into play. Young's[83] explanation is quite similar to that of Paramore except that the former holds that the curvature of the birth canal is important, a point that must be considered in view of the difference in the degree of curvature of the birth canal in lower forms and the human being. We should add that this driving force must

be properly directed by a uterine musculature working harmoniously through a coordinating mechanism.

On learning that the oviduct of the chicken rotates the egg and inversion of the egg frequently occurs in laying, that the small intestine imparts a spiral movement to a bolus, that the vagina of the rabbit manifests a tortuous spiral-like activity, that the uterus of the mare and dog usually rotates the fetus to a dorsosacral position for physiologic birth, it occurred to us that one horn may tend to rotate the fetus in one direction, and the other horn in the opposite direction. Unfortunately our x-ray plates gave us no information on this possibility which awaits further study. Obviously if this actually occurs in the bicornuate uterus, it is possible that such a phenomenon may have been retained in part by the primate uterus. If so, it has an important bearing on the cause of internal rotation.

Hence, we have searched the obstetric literature, and one of us (L. R.) has gone over his obstetric records to ascertain whether the human uterus ever manifests the property of "spiral action" which harmonizes with the longitudinal and circular forces to rotate the body and head. Since the rotation of the trunk by the uterus was discussed above, we shall not discuss that subject again, but we should like to point out that this factor must be kept in mind in regard to the interpretation of the points we are about to discuss.

Although internal anterior rotation generally occurs in the second stage of labor when the presenting part is fully within the confines of the pelvis, there are instances in which rotation occurs in the first stage and before the presenting part is under the full influence of pelvic factors. Stephenson[66] has stated that rotation may occur in the os uteri or on the pelvic floor, so that one cannot confine rotation to any limited portion. The fact, pointed out by Gillespie[82] and others[58, 83] that during uterine systole the presenting part rotates on its longitudinal axis and again recedes during uterine diastole frequently indicates that the resistances are not always fixed. (We have noted the same in the dog.) In footling presentation, Schmitt[60] argues that since the foot rotates while still in the pelvis, this rotation must be due to the rotation of the trunk by the uterus, a mechanism that has been suggested by Duncan[84] and Nagel.[85] Further, in conduplicatio corpora, the mechanism of the spontaneous delivery of the fetus is described by Douglas[86] as being due to uterine contractions, the fetus rotates about its vertical axis. One of us (L. R.) has observed that in occipitoposterior positions with the head engaged and with partial cervical dilatation, the head may rotate from a posterior position to the transverse and into an anterior position before complete dilatation of the cervix. This indicates that rotation may occur above the pelvic floor. This has also been observed by Zweifel,[63] Stephenson,[66] Cazeaux,[74] and Edgar.[78] Since rotation apparently occurs at the higher levels of the pelvic

cavity, during the first stage, it is unlikely that mechanical factors in the pelvis are concerned primarily.

The following points emphasize the rotation of the trunk by the uterus. In a roomy pelvis, superrotation of the occiput or shoulders not infrequently occurs (DeLee). It is difficult for us to believe that such a turbinal movement is due to the mechanical factors in the pelvis. Further, it is well known that if in persistent occipitoposterior positions in the second stage of labor, the head is rotated anteriorly manually or by a Scanzoni maneuver, the head will rotate back to its original position unless the back is rotated anteriorly or the head is held in place by the hand, a blade of the forceps, or with a Vulsella forceps on the scalp (DeLee). This difficulty is apparently due to the failure of the back to rotate anteriorly. Also one of us (L. R.) observed several years ago that in a diagnosis of O.L.P. or O.D.P., the back would occasionally be delivered in the opposite oblique. At that time this was ascribed to an error in diagnosis. In recent years, the diagnosis has been verified by roentgenograms made before delivery with the result that in a few cases the head would be delivered according to the diagnosis, but the back was not so delivered. This has caused us to study the mechanism involved. The mechanism is as follows: The head enters the pelvic inlet in an oblique diameter with occiput posterior. The body is placed with the shoulders (bisacromial diameter) in the opposite oblique, or the transverse. In a normal or *typical* occipitoposterior position, internal anterior rotation of the occiput results. A rotation of the shoulders in the same direction as the occiput occurs, which brings the shoulders finally into the same oblique diameter in which the occiput was at the onset of labor. In an *atypical* occipitoposterior position internal anterior rotation of the occiput results. The shoulders are rotated as in the typical case and the occiput is born. Now the shoulders undergo further rotation, or superrotation, in the same direction and the bisacromial diameter is born in the same oblique diameter in which it was when the occiput entered, but with the back anterior, i. e., the shoulder that was anterior is delivered posteriorly. Obviously the uterus must be primarily responsible for this rotation of the shoulders.

Summarizing the Foregoing Discussion.—The postural tone of the uterine musculature is the basic factor concerned in determining the presentation and position. The attitude of the head in the presence of normal cephalopelvic relations is due to the integration of three factors, namely, a harmoniously contracting uterus, the resistance to egress, and the unequally balanced two-armed lever that exists between the vertebral column and head. If the force transmitted through the fetal spinal column is misdirected by improper coordination of the upper uterine segment, or if the lower uterine segment or cervix is more atonic or yielding in one portion than another, the lever action will be modified or abnormal. The uterus, by rotating the fetal back anteriorly, assists anterior rotation of the occiput.

With the occiput right or left anterior, the levatores ani, the decreased resistance of the vulval slit, and the larger anteroposterior diameter of the outlet may rotate the occiput anteriorly. With the occiput in a transverse or a posterior position, and given a well flexed head, and a uterus that is coordinating and contracting adequately, the vertex on striking the pelvic floor is deflected anteriorly in a sagittal plane and a two-arm lever action operates in a "vertical" plane to rotate the forehead posteriorly and the occiput anteriorly about the vertex or occipitoaltoid articulation as an axis.

A mechanism for the typical and atypical delivery of the shoulders in occipitoposterior positions is offered.

A brief description of the comparative anatomy of the pelvis and the comparative physiology of the uterus in labor has been given. The results of a roentgenographic study of the delivery of the fetus in the dog are reported. On the basis of our studies, we conclude that in "lower animals" the uterus is primarily responsible for placing the fetus in a dorsosacral position for physiologic birth.

Certain human obstetric observations are discussed which may be interpreted as indicating that the uterus may rotate the trunk and head. Whether this is due to the existence of a uterine property of "spiral action" cannot be stated on the basis of the evidence at hand.

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DISCUSSION

DR. C. S. BACON.—Dr. Rudolph claims that rotation is due to uterine action and that the shape of the pelvis has little to do with it. The question I want to ask is how does the uterus act?

DR. D. A. HORNER.—From some of the pictures shown on the screen I have come to the conclusion that the mechanism of the fetal back is entirely different in human beings than it is in the lower animals. The human being has an erect position, while these x-rays are of animals in the horizontal position. In the human being the back follows the curve of the abdomen rather than the curve of the maternal back. It seems as if earlier in pregnancy the back follows the curve of the abdomen in lower animals, as in the human being, but changes during labor. In the human

being 95 per cent of the pregnancies are carried out at some stage or other with the back anterior or in the dorsopubic position.

The Sellheim experiments have shown that the curve of the canal plus the pelvic floor trough are responsible for the rotation of the fetal head and back.

Whether or not uterine action can rotate the baby depends on whether the bag of waters is ruptured. If the bag of waters is intact I doubt if the uterus can act on the baby floating inside the bag of waters and rotate it any way, anteriorly or posteriorly. With the bag of waters ruptured, the uterus contracts down on the fetus, often grips it tightly and may actually prevent its anterior rotation. The descent which is encouraged by rupture is responsible for whatever anterior rotation occurs.

Dr. Rudolph made one statement to which I must take exception, namely that, when the head is delivered, the shoulders may be above the inlet. The curve of the sacrum is 12 cm. and from the tip of the sacrum to the tip of the stretched perineum 12 cm. more making 24 cm. in all. As far as I know, no neck is that long and consequently no head could be delivered with the shoulders above the inlet.

DR. EDWARD L. CORNELL.—I rather hesitate to accept the statement that the uterus itself is capable of rotating the fetus, providing the bag of waters is intact. In exceptional cases it has been my observation that without any uterine contraction the fetus has rotated when the head is within the pelvis, but this has not been more than ten to fifteen degrees. If that is possible without a contraction, I would hesitate to say that the uterus itself can rotate a baby.

That the fetus can change its position of its own momentum without uterine contraction, I think is accepted. Spontaneous version is frequently seen in pregnancy and almost invariably the patient will tell you that at a certain time there was a great commotion in the abdomen. It has not been my fortune to see spontaneous version but I have always felt the activity of the fetus had something to do with rotation or with version.

DR. E. W. FISCHMANN.—In woman, because of the upright position and the absence of a tail, the tail muscles of the lower animals have been changed to the muscles of the pelvic floor which give support to the pelvic organs. Dr. Rudolph stated that the uterine contractions cause rotation of the fetus, but is not a pivotal point necessary for this rotation, probably the pelvic floor? I agree with Dr. Horner that the pelvic floor plays a most important rôle in the mechanism of labor, because we often find that in a multipara with a markedly relaxed pelvic floor there is no mechanism of labor at all, because the muscles of the pelvic floor are markedly separated and hence do not serve as a pivotal point for internal rotation, etc.

Dr. Rudolph speaks of the longitudinal muscle fibers; there are none in the human uterus for the fibers are arranged more or less haphazardly and interlace and cross each other.

DR. RUDOLPH (closing).—The work of Sellheim was based on purely mechanical principles of a double cylinder passing through a rigid curved canal. Dubois and Edgar's experiments seemed to corroborate the mechanical principles without attempting to evaluate the importance of the manner in which the directing force was directed. In labor we are dealing with a physiologic process in which both the fetus and the genital tract consist of vital structures, so that the experiments of Dubois and Edgar and the experiments of Sellheim, Moir and Young cannot be accepted as conclusive.

Dr. Bacon asks, what is the mechanism? According to Howell, we do not know the mechanism of peristalsis, pendulum movement and segmentation of the gastrointestinal tract. We accept it as a physiologic process irrespective of the mechanism

involved. The mechanism of the uterus is based upon physiology, even if we do not know the underlying mechanism.

We believe that the uterus by its coordination or incoordination will direct the longitudinal force in such a manner as to bring about flexion or deflexion. How does it occur? We do not know, neither do we know what brings about the onset of labor, but we accept the biologic knowledge that the onset of labor occurs in different species after a certain period of pregnancy.

Warnekros has demonstrated that the position of the fetal head is usually in some form of deflexion. Therefore, gravity or intrauterine pressure does not play a marked rôle in the mechanism of flexion of the fetal head during pregnancy. With the onset of labor the fetal head becomes flexed, which we must accept as being due to the uterine contractions in the normal mechanism of labor. This leads us to the premise that the distention of the uterus does not occur on account of the growing fetus, but is a physiologic coordination of the growth of the uterus to the demands of the growing fetus.

If evolution has any value in medical science, why should it not be related to obstetrics? If the uterus in the lower animals has rotatory power, why is it not logical to assume that perhaps the human uterus has retained that property? We have demonstrated that the pelvis was developed on account of physiologic demands, and that in the different species the mechanism of the delivery of the fetus was such that some vital structure had to determine the manner in which the fetus must be delivered. We believe that by the Law of Natural Selection the uterus has determined the mechanism by which the fetus is delivered in the different species, as well as in man.

In normal labor the head enters the pelvis in the oblique diameter, in the main, but in contracted pelves it attempts to enter in the transverse diameter to allow the smallest diameter of the head to pass through the anteroposterior diameter by either the biparietal or the bitemporal diameter. In a generally contracted pelvis the head attempts to pass into the pelvic cavity in the oblique diameter because it is still the largest diameter. Nature economizes the space in whatever manner it finds logical and that the directing active force is the uterus.

Dr. Fischmann asks about the pivotal point for the mechanism of rotation. The pivotal point is any part of the point of direction which comes in contact with the uterine wall directly or indirectly through the liquor amnii in order to form two opposing forces, and the angle formed will depend on whether the head remains stationary or is rotated anteriorly or posteriorly.

We believe that many cases are called disproportion on account of the deflexion of the head, which is due to the syndrome we have presented and is based upon uterine dysfunction. Wilson in a recent number of the *Journal of Obstetrics and Gynecology of the British Empire* writes, "Disproportion is usually the reason given when cesarean section is performed in an apparently normal pelvis and for some reason the head does not fit the pelvis well. It may be correctly ascribed to a certain amount of deflexion of the head due to or associated with imperfect functioning of the uterus." Therefore, our problem as obstetricians is to determine the manner to correct the uterine dystocia and not by means of increasing the number of cesarean section which increases morbidity and mortality.

We believe that through comparative obstetrics, we can study the physiology of parturition and as in the other branches of medicine apply that knowledge to the human uterus. We have considered too much the mechanical factor and should know more of the physiology of labor.

THE RESPIRATORY FUNCTION OF THE DETACHED PLACENTA

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THE interchange of gases through the walls of the chorionic villi, between the fetal and the maternal bloods occupies a prominent place in placental physiology. Except for this, death of the fetus would quickly supervene. In this paper evidence is presented which, I believe, will show that after separation of the placenta from the uterine wall oxygen may continue to be received and utilized by the fetal blood.

A review of the histologic structure of the chorionic villi will serve to clarify the subject matter at hand, hence without attempting a detailed description of the form and development of the placenta a brief outline of the facts pertinent to the discussion is presented. The chorion consists of two layers; an outer trophoblastic layer, and an inner mesodermal layer. The trophoblast in turn is made up of two layers; (1) an outer layer of nucleated protoplasm without cell boundaries called the syncytiotrophoblast or syncytium, and (2) an inner layer of cuboidal cells called the cytotrophoblast or layer of Langhans. The early chorionic villi consist at first of solid outgrowths of the trophoblast reaching out from the chorion over all its surface. Later these finger-like processes are invaded by mesoblastic tissue which then forms the core of the villi. Accompanying the ingrowth of mesoblastic substance is a system of blood vessels which in each villus consists, when developed, of an afferent arteriole, a mesh of capillaries, and an efferent venule. The arteriole carries mixed but essentially venous blood from a branch of the umbilical artery to the capillary tuft where it is purified to return through the vein as arterial blood. Demonstration of the facts that the umbilical arteries contain venous blood and that the umbilical vein contains arterial blood, together with the consideration that compression of the cord or abruptio placentae causes fetal asphyxiation, prove that oxygen is supplied to the fetal blood in the placenta,[1] and that adherence of the placenta to the placental site is necessary for the maintenance of the oxygen supply of the fetus in utero. After the second month the chorionic villi in contact with the decidua capsularis gradually undergo atrophy, while those in contact with the decidua basalis grow and develop, forming numerous branches and ramifications as well as increasing in size. Into these branches the system of blood vessels is likewise projected. The blood in the capillaries then is separated from the maternal blood in the intervillous spaces by the endothelium of the capillaries, the reticular mucoid stroma of mesoblastic tissue, the cytotrophoblast and the syncytium. At term the cytotropho-

blast has disappeared and the syncytium has become thinned out into a narrow band. Through these layers intervening between the fetal and maternal bloods the interchange of gases takes place by osmosis or cell activity, or both; although the preponderance of evidence indicates that it is mainly or entirely by osmosis.[2] Water and nutritive materials also pass through, and in the transference of protein substances in the form of amino acids, the vital action of the cells seems to play a more important rôle, but for the present thesis the gaseous exchange is our chief concern.

Soon after the birth of the baby the circulation in the cord ceases, the lungs at this time assuming the function of oxygenation of the blood. The pulsation of the umbilical arteries in the funiculus can no longer be felt and the activity of the placenta as a fetal organ is at an end.

It has been observed in a few instances when a baby was born with the placenta and unclamped cord expelled intact that the baby lived without respiration or asphyxiation for some time while the circulation through the cord and placenta continued. Schumacher[3] recently reported such a case in which a fetus miscarried in the fifth month and never breathed, and no artificial respiration was applied, yet the fetal heart beats continued for fifty minutes. In reporting this case the author advanced the opinion that the oxygen present in the blood in the fetus, cord, and placenta at the time of expulsion was sufficient to supply the needs of the fetus for the length of time specified, and that when this was chemically exhausted the heart stopped beating. However, he also suggested the possibility of "a sort of branchial respiration" by an intake of air through the placental villi, wounds (wound surface), and capillaries, maintaining the oxygen supply and the carbon dioxide waste. An incident of similar nature is outlined in the following case report.

CASE REPORT

The patient was an unmarried teacher, colored, twenty years of age. She had not reported for any prenatal care or supervision and at the time of her confinement was attended by an amateur midwife. Labor came on prematurely at about six months. After the birth of the baby she bled rather freely, the attendants therefore decided to apply for medical aid in the further handling of the case. On arrival I inquired about the baby and was told it had been born thirty minutes before, so my attention was turned at once to the mother who was bleeding freely enough to demand immediate treatment. It was approximately fifteen to twenty minutes or more before the condition of the baby could be investigated, or at a most conservative estimate forty-five minutes after birth. The infant was at the foot of the bed loosely covered with bedclothes; on lifting these the ovum was found to be intact, the bag of waters unruptured. The sac was broken and the baby lifted out. The heart was beating strongly, the color was normal and but little effort was required to induce respiration. The cord was clamped and severed. Breathing continued spontaneously but was rather shallow and crying was weak. The infant was wrapped in cotton, kept warm by external heat, and supportive and stimulative measures were instituted. He lived twenty-four hours, dying then because of respiratory failure and prematurity. Autopsy was not obtained.

COMMENT

A case with such sequence of events would never occur in a hospital where trained assistants are present to assume charge of a baby at birth, nor would it be likely to come about in a home delivery if the accoucheur were present during the second and third stages of labor; hence the case history itself being unusual, certain conclusions are suggested by a consideration of the clinical data which would not be apparent in the ordinary case as usually conducted.

In the first place, although the infant did not breathe for three-quarters of an hour, there was no evidence of asphyxiation nor of decreased or embarrassed heart action, so that it is a necessary deduction that during this time the baby was receiving his required amount of oxygen. The amount of blood in a newborn baby of average weight is approximately one-eleventh of the body weight, or about 280 gm. The amount of blood in the cord and placenta varies and no record of the accurate determination of its volume or weight is available, however the ratio between the amount in the fetus and the amount in the cord and placenta is somewhat more than 2:1. After compression of the cord the fetus may survive for five to ten minutes, rarely fifteen, and very rarely twenty minutes,[4] so that were the amount of fetal blood in the cord and placenta equal to the amount in the fetal body we should not expect the fetus to survive as long as three-quarters of an hour without reoxygenation of the blood. But with the usual length of time of survival, the cord and placenta would have to contain from four to five times as much blood as the fetus, whereas in reality they contain less than one-half as much. In cases of abruptio placentae with complete detachment, the length of time of survival of the fetus has not been determined, yet with the onset of symptoms violent fetal movements are felt by the mother and these are presumably the agonal struggles of the asphyxiated infant.

In the case reported the fetal body metabolism was active at at least the basal rate, and oxygen must have been consumed yet the total volume of blood in the fetus, the cord and placenta would be insufficient to supply the requisite amount of the gas for the length of time specified without reoxygenation. Therefore, we must conclude that the fetal circulation was receiving oxygen from some outside source. As the fetal organism was consuming rather than generating oxygen the source of supply must be looked for in the cord or in the placenta. The cord was enclosed in the amniotic sac and surrounded by amniotic fluid, its blood vessel walls comparatively dense and these covered by a greater or less thickness of Wharton's jelly and overlaid with a layer of ectoderm. Furthermore, even were it possible for oxygen to penetrate these structures only a small portion of the blood corpuscular surface would be exposed to it, hence oxygenation would be incomplete. This then leaves the placenta as the only source of the oxygen supply. Here we have the blood in the capillary meshes of the villi separated from the air by a single layer of endothelium, a small amount of mesoblastic stroma, and a thinned out syncytium; structures whose permeability to oxygen and carbon dioxide as exchanged between maternal and fetal bloods has long been recognized. There is this difference however, that oxygen exists in the maternal blood in a combined form (oxyhemoglobin), and in the air as a free gas mixed with other gases. But the oxygen in oxyhemoglobin is so easily dissociable that the oxygen tension is regulated by the oxygen pressure in the surrounding atmosphere just as though it were merely in solution,[2] and transference of the gas is by dialysis through the intervening structures. The condition in the case discussed here is analogous to that obtaining in the respiring lung where the blood in the capillaries is separated from the air by the thin walls of the capillaries themselves, a small amount of delicate connective tissue containing the capillary network, and the simple squamous epithelium lining the alveoli and alveolar air sacs. So a careful evaluation of the data presented leads to

the conclusion that in this case a gaseous exchange took place between the atmospheric air on the one hand, and the blood circulating through the capillaries of the chorionic villi on the other.

The cause of the premature labor was not ascertained but the gross appearance of the placenta indicated no abnormality in its structure nor any disease of its tissues, and though generalizations are hazardous it seems justifiable to suppose that any normal placenta under similar conditions might function in the same manner.

Schumacher[3] in his paper points out the importance of the placental blood in improving the prognosis in asphyxia or of threatened asphyxia of the newborn, and shows the value of his observations in supplying a hitherto unrecognized reason for not clamping the cord in such cases while the circulation continues through it, and also in pointing out the importance of starting artificial respiration before compressing the umbilical vessels.

SUMMARY

1. The passage of oxygen through the walls of the chorionic villi from the maternal to the fetal blood and of carbon dioxide from the fetal to the maternal blood have long been accepted by physiologists as proved phenomena.

2. That the same interchange of gases may occur between the fetal blood and the atmospheric air after detachment of the placenta from the uterine wall is not so widely recognized.

3. A case is reported in which the assumption of such a gaseous interchange is requisite to a rational explanation of the sequence of events in the case history.

4. This function of the detached placenta may have a practical application in the treatment and prevention of some cases of asphyxia neonatorum.

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Boggan, R. H., and Wrigley, A. J.: Rupture of Ovarian Blood-Cysts Simulating Acute Appendicitis. Lancet 221: 1068, 1931.

The authors report 13 cases of this condition, the right ovary was affected in ten. They imply that the ovarian hemorrhage is an exaggeration of the normal physiologic mechanism of the rupture of the Graafian follicle. The essential diagnostic differences favoring ruptured ovarian blood-cyst are: the sudden onset of severe lower abdominal pain in relation to slight trauma; the good general condition of patient in spite of its duration; and marked lower abdominal tenderness without marked muscular rigidity.

They advise exploratory laparotomy if the diagnosis is uncertain (usually) and recommend at operation enucleation of the hemorrhagic area.

H. Close Hesseltine.

THE BERCOVITZ TEST FOR PREGNANCY

A Report of 260 Cases

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THIS investigation of the pupillary reaction described by Bercovitz in 1930[1] as a diagnostic aid in pregnancy, was undertaken on the obstetric service of Dr. E. L. King, in an effort to determine the reliability and value of the test.

The technic as presented by Bercovitz consisted of instilling into one eye of the patient a few drops of her own blood. At first serum was used, but this was later modified to citrated whole blood. Pregnancy was indicated by either a dilatation, a contraction, or an alternation of the two, in contrast with the other eye in which there was no change. His studies revealed that the patient's blood was capable of producing the same reaction in the eyes of nonpregnant individuals and in rabbits and cats. Precautions had to be taken before the test that the pupils were equal in size, and that the two eyes were evenly illuminated by a soft yellow light. The quality of the light and its intensity were particularly stressed. Of 72 nonpregnant women, not one gave a definite positive test. In 72 observations on 68 pregnant women, 80 per cent showed a definite pupillary change, 4 per cent a doubtful change, with the remainder giving no reaction.

Gordon and Emmer[2] partially confirmed the test, using citrated blood. Their results showed a positive reaction in 64 per cent of 90 pregnant women. They made the statement, without data, that no nonpregnant woman gave a positive reaction. White and Severance[3] performed the test on 58 pregnant women, of whom but 19 gave a positive reaction, and on 15 nonpregnant women, of whom 3 did respond positively.

In the series, herewith reported, citrated blood was used at first, but soon the technic was simplified by taking from the finger several drops of blood in an ordinary medicine dropper and transferring it directly to the conjunctival sac. The light used was either a low power electric bulb in a darkened room, or else daylight through heavy yellow shades. The pupils were examined first for equality and reactivity, and the patient was forced to fixate on a distant point to obviate accommodation changes.

The objections to the test are many. Fig. 1 illustrates the relative size of the pupils in the ordinary positive case. The end-point is very hard to read, and the reaction, furthermore, is relatively transitory. The matter of illumination is of such importance that the experimental error may be very large. There does not seem to be available any means of making precise measurements or a permanent record, and hence the variable factor of the personal equation must be depended upon. The test is not adapted to individuals with dark eyes, particularly negroes. Herewith are presented, however, the results of this investigation with the technic in its present status.

All three types of reaction pointed out by Bercovitz were observed. These appeared in from a few to thirty seconds and persisted from one to

about three minutes. The relative frequency in 73 positive cases was as follows:

Dilatation	27
Contraction	28
Alternation	18

In the series there were 107 cases of definitely proved pregnancy, of which 93 came from the prenatal clinic and 14 from the gynecologic wards, representing either threatened or recent incomplete abortions.

The patients were studied in respect to the following details: age, parity, length of gestation, and nervous constitution. There were several cases each of thyrotoxicosis, syphilis (both treated and untreated), dia-

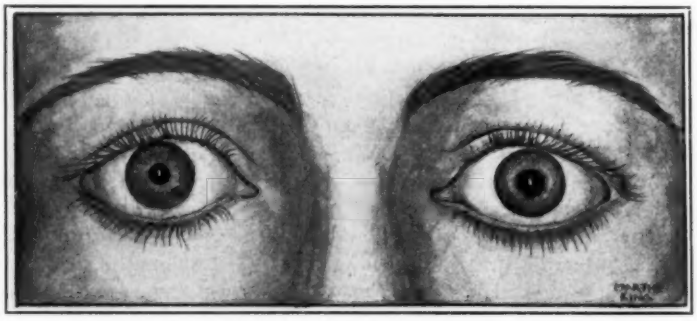

Fig. 1.—Showing the difference in the size of the pupils in the ordinary positive reaction of the Bercovitz test in pregnancy.

betes, fevers of various origins, and toxemias of pregnancy. Neither the correctness of the result nor the type of reaction was influenced by any of these factors.

Numerous positive tests were obtained as early as seven or eight weeks after the last menstrual period, often before pregnancy could be diagnosed clinically with any certainty; these cases were all confirmed later, however. In two cases negative results were obtained at eight weeks, with positive reactions appearing at the tenth and twelfth weeks respectively.

On the other hand an observation was made that is disturbing statistically, namely, that in the same woman the test might be positive on one occasion, negative on another, and positive again later, but with a different type of reaction. The conditions under which the testing was done were almost identical, but the factor responsible for this variability and for the false negative reactions is as mysterious as the cause of the phenomenon.

The results obtained with these known pregnant women are given in Table I. It appears that not more than two out of three pregnant women will give a clear-cut positive reaction with this test.

EPINEPHRINE

Bercovitz suggested that the reaction might be due to an epinephrine-like substance, and found that epinephrine (1-1000) when dropped into

the eyes of the same series of pregnant women gave 76 per cent positive, 2 per cent doubtful, and 20 per cent negative results. He noted that 2 of 98 nonpregnant women gave a positive reaction.

In this investigation, epinephrine gave no positive reaction in 40 nonpregnant women. Table II summarizes the results in 45 pregnant women. It is seen that the results with epinephrine were not nearly so good as with

TABLE I. REACTIONS WITH KNOWN PREGNANT WOMEN

	OBST.		GYNEC.	TOTAL 107 CASES		BERCOVITZ 72 CASES	GORDON & EMMETT 90 CASES
Positive	61	66%	12	73	68%	80%	64%
Doubtful	11	12%	1	12	10%	4%	13%
Negative	21	22%	1	22	21%	16%	21%

TABLE II. COMPARISON OF RESULTS WITH BLOOD AND EPINEPHRINE IN PREGNANT WOMEN

BLOOD	EPINEPHRINE		
	POSITIVE	DOUBTFUL	NEGATIVE
Positive (27)	15	0	12
Doubtful (9)	3	3	3
Negative (9)	4	0	5

blood, although the series is too small to discuss percentages. But in four of these pregnant patients in whom the blood was negative, and in three in whom it was doubtful, the epinephrine reaction was distinctly positive. On the other hand it was interesting to note that in four of the confirmatory positive tests, the type of reaction was different. In general, contraction was noted as often as dilatation.

The concept of the cause of the reaction being an epinephrine-like substance does not appear to be tenable. The typical epinephrine reaction is dilatation. Consultation with several physiologists revealed the information that epinephrine ordinarily affects the pupil only in the presence of a lesion of the cervical sympathetic system and in some cases of glaucoma.

PUERPERIUM

Bercovitz stated that the reaction disappears in from three to seventy-two hours after labor. Unfortunately, in this investigation it was not possible to follow in the wards all the women seen in the clinic. The results of 45 tests performed during the puerperium are given in Table III.

TABLE III. RESULTS OF TESTS DURING THE PUERPERIUM

	6-24 HOURS	24-48 HOURS	THIRD THROUGH NINTH DAY
Positive	5	1	1
Doubtful	2	0	4
Negative	12	4	21

Similar to the observation made in the prenatal clinic, one woman with a threatened abortion gave no reaction before delivery, a positive six hours after delivery, and a negative reaction two days later.

Two cases must be taken up separately as they have not been included in any of the tables because of the difficulty in classification. One woman had delivered thirteen months before, was lactating, and had not menstruated in the interim. She was definitely not pregnant, but gave a positive reaction. The other woman had given a positive reaction on the eighth day postpartum; three months later she gave a positive reaction, although of a different type. She had menstruated once in the meantime, and was definitely not pregnant. These two constitute false positives and weaken the value of the test in situations where it is most needed.

NONPREGNANT INDIVIDUALS

The nonpregnant individuals were divided into three groups: gynecologic cases, males, and normally menstruating young females.

Of 26 gynecologic patients, 5 with simple amenorrhea, 2 at the menopause, 2 with cancer of the cervix, and 17 with uterine bleeding where no decidual tissue could be demonstrated, all gave definitely negative reactions.

TABLE IV. RESULTS OF TESTS ON NONPREGNANT INDIVIDUALS

	GYNEC.	MALES	FEMALES	TOTAL	
Positive	0	0	2	2	2%
Doubtful	0	3	8	11	10%
Negative	26	18	49	93	88%

On the other hand, of 20 men tested, only 18 were distinctly negative. One man had a questionable contraction, and another, on two different occasions, showed considerable activity in the tested pupil in contrast to the control pupil, although the reaction was not definitely positive. Each of these two young men was of the nervous type, without, however, any signs of endocrine disorder.

Bercovitz, and Gordon and Emmer, failed to obtain a positive reaction in their normally menstruating groups. It was felt for a time, particularly after the excellent results with the gynecologic patients, that a positive reaction definitely indicated pregnancy. The two special cases referred to above, and the reactions in the young men cast grave doubts on this hope. This was confirmed by a series of young women who were menstruating regularly, and who, by reason of intelligence, position, and training, could be reasonably assumed to be not pregnant, although they were not examined. They were studied in relation to nervous constitution, normality of catamenia, and the time of the test in the menstrual cycle. None of these factors seemed to have affected the results. Some girls giving a doubtful reaction when menstruating, when reexamined a week or two later were definitely negative; on the other hand, some girls giving a doubtful reac-

tion in the middle of the cycle were negative when they menstruated. Of this series, 2 showed positive reactions and 8 gave doubtful tests.

The results are summarized in Table IV to which must be added the two false positive reactions at three months and thirteen months respectively after delivery.

SUMMARY

1. The value of the Bercovitz pupillary reaction in pregnancy, although it is exceedingly simple, is greatly impaired by the difficulty in reading the result and by the fact that much depends on the personal equation of the observer.

2. In 107 cases of proved pregnancy a positive result was obtained in 68 per cent, a doubtful response in 10 per cent, and a negative result in 21 per cent.

3. Epinephrine, 1-1000, will give similar reactions, to some extent. In 7 cases out of 45, epinephrine gave a correct positive result when the blood test was either negative or doubtful.

4. The reaction is not constant in the same woman at different examinations.

5. The reaction disappears early in the puerperium in most but not all cases.

6. In 108 tests on nonpregnant individuals there were 4 false positive responses and 11 doubtful reactions.

CONCLUSIONS

From the data presented here it must be concluded that the test, using the technic of Bercovitz, is not reliable enough to be of value in doubtful cases of pregnancy. The reaction is empirical in nature; it lacks precision, and is liable to error in interpretation because of technical difficulties and the personal factor.

On the other hand the phenomenon is interesting and merits investigation in the hope that the explanation of it will throw more light on the physiology of pregnancy.

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VARICOSE VEINS OF PREGNANCY*

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IN THE city welfare clinics of Los Angeles for prenatal patients, directed by Drs. Boehm and Pott, it was found that of 110 consecutive patients, 23 had outright varicose veins, and 27 had teliangiectases of the legs. Thus the pregnancy patients had varicose veins in one case out of every five, and if we add teliangiectases, there were incipient venous dilations in almost half the prenatal cases. This indicates that varicose veins in the prenatal patient are a problem of importance.

ETIOLOGY

There is a notion amongst obstetricians, dating from Pierre Dionis, 1707, that these veins of pregnancy are due to pressure by the pregnant uterus on the external iliac or common iliac veins in the pelvis, obstructing the venous flow.[1] This notion is called in doubt by four considerations. First, the varicose veins have been reported as beginning early in pregnancy before the uterus had enlarged and risen sufficiently to reach the external iliac veins.[2] Secondly, it has been reported that in cases where the fetus died in utero but was not expelled, the veins regressed at once, before the uterine mass could have involuted sufficiently to relieve pressure on the iliac veins.[3] These two statements need verification by further observations by obstetricians. Thirdly, when the varicose superficial saphenous vein was entirely obstructed by a ligature in 381 patients, the veins were not made worse but were improved.[4] If the whole trouble were caused by obstruction due to pressure by the uterus on the external iliac vein this could not occur. And fourthly, the majority of pregnant patients in the early stages of vein disturbance show small varices with a distribution scattered all over the legs, and not confined to the main tributaries of the great saphenous. Recently I saw in consultation a primipara, pregnant for four months, with enormous varicose veins high on the side of the body over the right kidney region. They had been present before pregnancy as congenital anomalies but had become much worse since she had become pregnant. It would be difficult to explain their increase at this location because of pressure by the uterus on the iliac veins. All these considerations point to some other cause.

It is likely that this cause will be discovered through the study of a phenomenon which no one apparently has yet noticed: namely, that in pregnancy, venous dilatation is only part of a general dilatation of all the smooth muscle tubes of the woman's body. There are four such smooth muscle tubes: the müllerian duct tube, the wolffian duct tube, the gastro-

*Read before the Los Angeles Obstetrical Society, February 9, 1932.

intestinal tube, and the blood vessel tube. In pregnancy the smooth muscle in all four of these tubes loses its tonicity.

In the wolffian duct tube, the early dilatation of the ureters was described by Cruvelhier[5] as early as 1843, and has been many times confirmed. I quote from Olshausen,[6] Prutz,[7] Lohlein,[8] Carson,[9] Hofbauer,[10] Seng,[11] Mandruzzatto[12] Gellhorn[13] and Draper[14] who report in almost identical words, as follows:

"During pregnancy the ureters always dilate. The dilatation is demonstrated about the eighth week and is very marked. The ureteral dilatation cannot be ascribed to pressure from the enlarged uterus because it has been observed in the first weeks of pregnancy. In a minority of the women the ureters, having once been dilated, return to normal, but in a relaxed state, after the ninth to twenty-fifth day postpartum. In the great majority the dilatation persists after the twenty-fifth postpartum day, and continues in a lesser degree over a prolonged period of time. Our studies have impressed us with the tissue factor of each individual woman."

Not only is there dilatation, but also a hypertrophy. Hofbauer has shown the stimulus of pregnancy leads not only to hypertrophy of the uterus, but also hypertrophy of the muscle in the trigone of the bladder, in the lower end of the uterers and in the vagina. There is this same hypertrophy of the muscle in the walls of the veins.

In the gastrointestinal tube there is, in pregnancy, a similar loss of tonus in the smooth muscle. Gellhorn[15] has found that the intestines like the uterus have a lowered tonus in pregnancy and Alvarez[16] after work on animals finds there never was much question about the existence of a gradient from duodenum to ileum or about its reversal, or flattening in pregnant animals. Even the muscle of the gall bladder derived embryologically from the intestinal tube loses tonicity and power to contract and empty.[17]

In the blood vessel tube, the arteries as far as blood pressure indicates, undergo this influence only slightly for reasons of obvious biologic necessity, but the tendency to dilatation of the veins is before you. Thus far in recognizing venous dilatation in pregnancy as a part of a generalized dilatation of smooth muscle we are on firm ground of fact.

When, however, we turn to search for the explanation of this fact, the path is not clear. The fact that this loss of tonicity is not limited to the veins but is generalized, points to some physiologic influence. Meisen[18] believes this is a toxemia of pregnancy. Possibly Henderson's recent work[19] may show some relation of the loss of smooth muscle tonus to the respiratory activity in pregnancy. The French clinicians, Sicard,[3] Gaugier,[20] Delater,[21] and Forestier[22] have been convinced that it is due to a change in endocrine equilibrium. Forestier and Gaugier believe that it is due to insufficiency of posterior pituitary secretion. Unfortunately the French school has shown inadequate proof of their position.

In favor of such a hypothesis, I can gather only this fragmentary evidence:

The posterior pituitary extract is probably more than a mere accidental content of the dead protoplasm of the pituitary, for Krogh[23] has shown that in the horse it is constantly secreted by the living pituitary into the blood stream through the internal jugular vein. This secretion when injected artificially into the body, causes contractions in the muscle of such müllerian duct derivatives as the uterus and powerful contractions of such wolffian duct derivatives as the ureter[24] and bladder.[25] Although its action on the intestinal tract under abnormal conditions may be variable[26] every practical clinician knows that in nearly every normal individual the bowel movements which follow its use point to intestinal contractions. There has been some evidence to show that it raises the tonus in the arteries and veins.[27]

We cannot conclude that just because it is probably secreted normally into the circulation, and because given artificially it causes contractions of smooth muscle, that therefore it is the normal physiologic stimulus to the tonus of these muscles. A beginning in this direction however has perhaps been made by Krogh working on the lower animals, who found by experiments on the capillaries and melanophores of frogs that in the case of the capillaries there is a substance circulating in the blood which does maintain the normal tonus of the smooth muscles in the walls of the capillaries, and without which the tonus is lost, and that this circulating substance is identical with posterior pituitary secretion!

When we turn for evidence to show that the action of the posterior pituitary secretion is diminished in pregnancy a number of experiments are significant. Knaus[28] found in experiments on rabbits that in them it was possible after the eighteenth day of pregnancy to induce an abortion with very small doses of posterior pituitary extract and ascribes the inertness of the uterine contractions in the first half of pregnancy to the hormonal action of the ovary neutralizing or paralyzing the hormone of the posterior pituitary. Broun is so confident of this lack of pituitary secretion during pregnancy that he administers it in cases of toxemias of pregnancy. Krogh[23] found that although experiments with human blood were unsatisfactory, that its concentration seemed lower in the later stages of pregnancy than during labor. Finally Siegert[29] in experiments on the excised uterus of rats and guinea pigs has shown that the follicular hormone which everyone now knows is present in the blood during pregnancy in enormous amounts, checks or entirely nullifies the posterior pituitary secretion.

I hope that I shall not be quoted as accepting this belief of the French school that disturbance in the endocrine balance causes venous dilatation. I am merely mentioning it as a hypothesis deserving further study.

A new instrument for measuring venous pressure is being perfected by Eyster and this may enable us to determine directly the effect of posterior pituitary secretion and the hormones of pregnancy on the veins.

It is hoped that not only the pharmacologists but the obstetricians and urologists may cooperate to help to solve this problem.

ROUND GARTERS IN PREGNANCY

For many years obstetricians have warned the pregnant patient not to wear round garters lest they cause varicose veins.

The question as to whether the obstetric patient should be warned not to wear round garters depends upon the direction of the blood flow in the superficial veins of her legs. If there is an important circulation in these veins upward, then it is right to forbid the wearing of round garters lest they obstruct the upward flow and cause the veins to bulge below the garters. On the other hand if the blood flow in the superficial veins is downward in a hydrostatic dead weight away from the heart toward the feet, then the round garters are a very good thing for the patient, for they obstruct no upward flow and hold back the heavy downward pressure of blood which would tend to bulge them out in dilatations. Experiments by Barber[30] brought contradictory reports but rather indicated that there is an upward flow in the superficial veins. Fluoroscopic examination of the veins after the injection of lipiodol as a radio-opaque medium by Magnus, Sicard and McPheeters have shown the flow emphatically downward toward the feet. Schmier[31] has thought this might be an error due to the great weight of the lipiodol which might carry it downward against the direction of the blood flow. He repeated this work with lipiodol especially prepared of a concentration to give a specific gravity equal to that of normal blood. His results with such a preparation showed that in some patients with varicose veins *vis a tergo* pressure from the capillaries slowly forced the blood upward against the dead weight of hydrostatic pressure. In other patients he found exactly the reverse to be true and the blood flow in their superficial veins was downward, then through communicating veins low in the leg to the deep veins, and thence upward.

I have used uroselectan (iopax) as a radio-opaque medium. I have experimented mixing it with blood in a glass tube and find it diffuses, mixing with the blood, and does not sink through the blood. Fig. 1 shows a normal vein into which 1 c.c. of uroselectan has been injected just above a valve. The valve has efficiently prevented direct downward flow. There is some downward flow by way of the communicating veins until numerous small valves are reached when the downward flow is halted. There may be some upward flow due possibly to the mere mechanical pressure conveyed from the piston of the syringe but whatever upward flow there may be is at any rate a most feeble affair for although this picture was taken half a minute after injection the shadow of the uroselectan in the vein is still there and has hardly moved upward an inch.

Further x-ray studies indicate that in the normal person in the standing position there is very little upward flow in the superficial veins, and

that there is a definite downward flow below the great valve in the saphenous just below the knee. During exercise the circulation, possibly upward, may be increased but veins are not distended by exercise. If a distended segment of a normal or varicose vein is isolated between two rubber bands and the patient is asked to walk, the full superficial segment is soon emptied. The recumbent position is also unimportant in this problem, patients remove their garters when they go to bed, and the superficial veins always empty anyway.

Fig. 1.

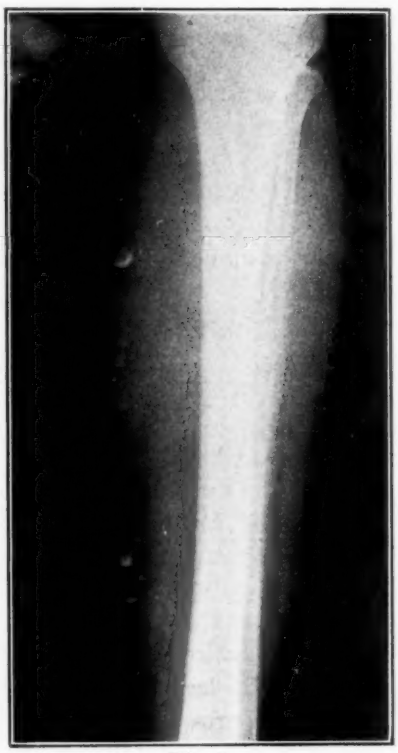

Fig. 2.

Fig. 1.—The circulation in the normal vein above the great valve shown twenty-five seconds following the injection of 0.5 c.c. of 33 per cent uroselectan.
Fig. 2.—Downward flow in varicose veins of multipara in the tenth month, twenty seconds after injection of uroselectan. Double positive Trendelenburg.

The next picture (Fig. 2) shows the left leg in which there was a double Trendelenburg, which means that by a clinical test it had been shown that the valves of this leg were incompetent in both the superficial veins and in the veins communicating between the superficial and deep veins. The shadow in the leg even in the instant after injection is moving downward from the point of injection at the finger tip. There is no sign of any upward flow even though there was time for the circulation to pass upward before the finger was applied.

This next picture (Fig. 3) taken one minute and twenty seconds after

injection shows the shadow passing not only downward but through a communicating vein with an incompetent valve into a straight deep vein by which it is now ascending rapidly upward.

Fig. 4 shows the other leg in which there was a single positive Trendelenburg, which means that clinical tests had indicated that the valves in the superficial veins were incompetent but that the valves in the communicating veins were competent. This picture taken immediately after injection shows no upward flow but a rapid downward flow in these super-

Fig. 3.

Fig. 4.

Fig. 3.—Circulation through communicating vein and up into the deep vein in multipara in tenth month, one minute and twenty seconds following injection of uroselectan. Double positive Trendelenburg.

Fig. 4.—Downward circulation in varicose vein of multipara in the tenth month immediately following injection of 0.6 c.c. uroselectan. Single positive Trendelenburg.

ficial varicose veins. Pictures taken twenty and eighty seconds later show the uroselectan scattered through varicose veins all around the leg to the ankle and still staying there.

It should be evident that in this pregnant patient with severe varicose veins, in the standing position there was no upward flow in these veins to be impeded by round garters.

But can the round garters obstruct the upward flow in the deep veins?

Again the answer is "no." I know because I have applied a tourniquet very tight, much tighter than a patient would think of wearing a garter, and yet the opaque medium is carried away in those deep veins so rapidly that it is difficult to take an x-ray quickly enough to catch it on the plate. The deep veins are buried too deeply near the interosseous membrane under pads of thick muscle of the calf and thigh to be affected by the pressure of round garters.

Fig. 5.—An old but effective relief of varicose veins. Compare the round garter.

As far back as 1844, Colles invented a vein truss, which was a spring, encircling the thigh like a hernia truss but with the pressure pad over the saphenous vein near the fossa ovalis to relieve varicose veins by shutting off and thereby relieving the downward pressure from above. He noted that this was particularly useful in pregnant women.[32]

It was an old trick for years for clinicians treating varicose veins to apply strips of adhesive around the leg, like a firm, round garter.

Complete obstruction of the superficial veins by ligation, has been

known to improve them rather than to make them worse. It was practiced by Paulus of Aegina, 660 A.D.,[33] Ambrose Pare, 1579,[33] by Velpeau,[33] and Trendelenburg.[33] Berntsen[4] in patients with a single positive Trendelenburg obtained improvement in 80 per cent by high ligature, and Jeannel obtained thus a complete cure in 28 per cent of 83 patients. Closing off the lumen of the vein above, did not cause venous dilatation below, it cured the varicose veins! More recently de Takats has been able to check the progress of the development of varicose veins in pregnant women by this same method.[34]

The intelligent patient cannot help being confused when the surgeon specializing in varicose veins applies pressure over the veins, or even ligates them, while her obstetrician forbids the possible obstructive pressure of round garters!

It is conceivable that in patients with a tendency to edema, round garters may be tight enough to obstruct lymphatics and make the edema worse; but I have been speaking of varicose veins. I want to mention also that superficial veins around the foot have a very active circulation upward.

My own opinion is that in the normal person in the standing position round garters may have a theoretical effect in obstructing a sluggish upward venous flow through superficial veins; but I doubt whether this is of much importance. I have never found any evidence to prove that varicose veins have been so caused. In the patient who already has severe varicose veins, I am sure that round garters not only do her no harm but may be of important benefit to her.

The incontestable mass of evidence of cures of the veins, by complete obstruction by ligating the vein makes me reluctant to forbid round garters to pregnant patients who already have varicose veins.

Did we never hear of straining out the gnat and swallowing a camel; some obstetricians meticulously forbid round garters and then order an elastic stocking!

TREATMENT OF VARICOSE VEINS IN PREGNANCY

Objection to treatment of varicose veins in pregnancy is very old. Ambrose Pare wrote of them in 1579 "women with child are commonly troubled with them by reason of the heaping together of their suppressed menstrual evacuation. It is best not to meddle with such as are inveterate for of such being cured there is to be feared a reflux of the melancholy blood to the noble parts whence there may be danger of maligne ulcer, a cancer, madness or suffocation." Pigeaux warned of a case of abortion in a cook, following the bandaging of varicose veins.[35]

It was therefore a surprise when McPheeters[36] had the courage to read a paper vigorously urging the injection of varicose veins of pregnancy. His paper was based on a series of 46 patients. Most of them had had pain beginning in the fourth month of pregnancy, in some cases so severe as to

make them partial invalids. Most were treated within a period of ten days in the fifth month. Ninety-two per cent were relieved, and 89 per cent said that under similar circumstances they would wish their friends so treated. It was urged: First, whatever relieves pain cannot be called meddlesome obstetrics; secondly, elastic stockings are unsanitary and linen mesh bandages will not stay on above the knee; thirdly, injection treatment is harmless and by obliterating the varicose veins may prevent the occurrence of phlegmasia alba dolens.

If a pregnant patient is in serious pain or discomfort I see no objection to allowing relief by the simple expedient of injecting the veins. As to the question of preventing milk leg by previous varicose vein injection I know by clinical experience that varicose veins do develop phlebitis with a frequency not found in normal veins. However, phlegmasia alba dolens most often begins in the deep veins of the leg and later involves the superficial veins. General treatment of varicose veins of pregnancy as a prophylactic against phlebitis would not be advised.

In the majority of light cases it is preferable to wait till after delivery and see if the varicose veins will not regress spontaneously. However, the treatment is indicated in patients with serious distress during the fourth to seventh months of pregnancy.

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CONGENITAL PNEUMONIA OF THE STILLBORN AND THE NEWBORN*

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IN CONSIDERABLE numbers of stillborn as well as newborn children who do not survive more than a few hours after birth, sufficient cause for death is often not found.

Thomson tried to ascertain the most prevalent pathologic causes of stillbirth by way of a widely distributed questionnaire but found that most diagnoses were not made on the evidences of autopsies. The macroscopic findings of McDowell's autopsies on stillborns were more illuminating however, inasmuch as he showed that 23½ per cent of his cases died of pathologic conditions found in the lungs. Still more interesting is the report of Hook and Katz who reported that in twenty-two cases of congenital pneumonia, only two could be diagnosed on the gross pathologic findings, whereas in the rest of the cases the evidences of pneumonia could be found only by microscopic examination.

Within twenty-one months of the years 1929 and 1930, thirty-nine cases of stillbirths and early deaths of newborn children were surveyed by me with the following result: Six were macerated fetuses which did not lend themselves to further investigation. Nine were premature stillborns and did not show any other pathology save that of underdevelopment and marked general debility. Two were stillborns showing severe malformations of the central nervous system (encephalocele) and two cases revealed cerebral and intraperitoneal hemorrhages respectively.

In 3 of the remaining 20 cases the lungs were of dark walnut color, especially in their posterior aspect, liver-like in consistency and from the cut surface of these dark firm parts, a granular material could be scraped off with the knife, so that the macroscopic diagnosis of bronchopneumonia could be made. In these three cases unfortunately, no histologic examinations were done. However, in view of the fact that two were stillborn and one infant lived only seven hours, there can hardly be any doubt about the fact that these three cases of pneumonia were of congenital origin.

The remaining 17 cases were examined histologically and 9 out of this group were diagnosed as pneumonias. In the other 8 no inflammatory changes were present. The individual reports follow:

CASE 1.—The alveoli were distended and filled with serous exudate, massive amniotic material and occasional desquamated cells. The blood vessels and septa showed margination and beginning emigration of leucocytes. Diagnosis: aspiration, incipient pneumonia.

CASE 2.—The lung was fairly well aerated, but the alveoli were separated by broadened septa. The septa showed hyperemia and leucocytic infiltration. Many

*Read before the Brooklyn Gynecological Society on May 6, 1932.

alveoli were plugged with cellular exudate. Similar exudate was present in the bronchi. Amniotic matter was found in the alveoli and bronchi. Diagnosis: aspiration; bronchopneumonia.

CASE 3.—Identical with the previous, but larger foci of pneumonic infiltration. Diagnosis: aspiration, bronchopneumonia.

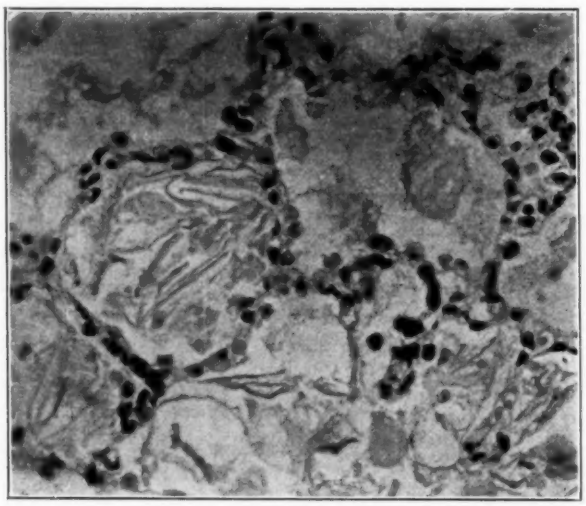

Fig. 1.—Distended pulmonary alveoli filled with amniotic material.

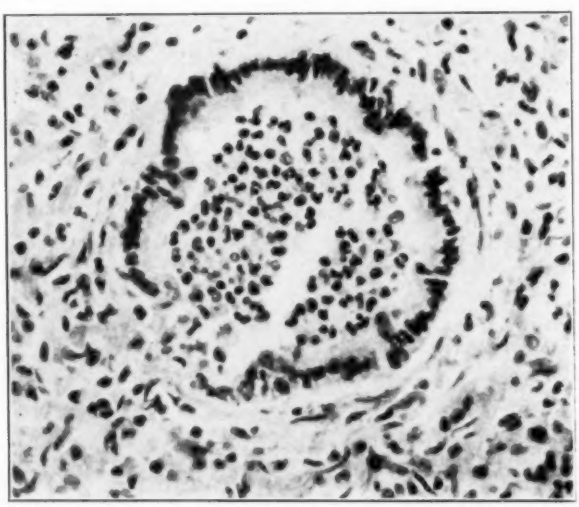

Fig. 2.—A section from a case of congenital pneumonia, showing a small bronchus filled with purulent exudate.

CASE 4.—Only a few alveoli contained air, the others were collapsed or filled with cellular exudate, mostly of polynuclear kind. Many of these intraalveolar plugs enclosed amniotic material. The larger bronchi were filled with purulent exudate in which amniotic material was present. Diagnosis: aspiration; coalescent bronchopneumonia.

CASE 5.—Diffuse hemorrhagic infiltration of the lung, with almost complete obliteration of the pulmonary structure was present. Numerous amniotic scales were embedded in the structureless substance. In some places there was an accumulation of cells, some of which were polynuclear leucocytes, others wandering cells with distorted nuclei. Diagnosis: aspiration; hemorrhagic infiltration; focal bronchopneumonia.

CASE 6.—Engorgement of the blood vessels and diffuse hemorrhagic infiltration of the lung tissue. The alveoli contained besides blood and desquamated cells also large amounts of amniotic material. Diagnosis: aspiration; hemorrhagic infarction.

CASE 7.—The capillaries as well as the larger blood vessels were engorged; the lung was partly atelectatic. The aerated alveoli contained some coagulated albuminous matter in which amniotic scales were seen. Diagnosis: atelectasis; congestion; aspiration.

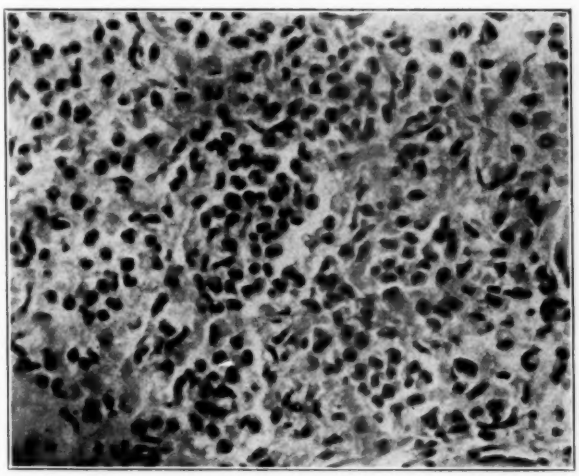

Fig. 3.—A section from a case of congenital pneumonia, showing catarrhal exudate and massive amniotic material in the alveoli.

CASE 8.—Only partly aerated lung tissue was seen. No evidence of inflammation. Amniotic matter was present in the alveoli. Diagnosis: partial atelectasis; aspiration.

CASE 9.—The capillaries and the larger blood vessels were engorged. There was no evidence of inflammation. Unusually massive amniotic matter was present in the alveoli. Diagnosis: atelectasis; aspiration.

CASE 10.—The alveoli were filled with desquamated epithelium and occasional leucocytes. Abundant amniotic material was also present and cellular infiltration of the septa. Diagnosis: aspiration; catarrhal bronchopneumonia.

CASE 11.—The lung was atelectatic almost throughout. There were a few alveoli however, containing a fibrinous exudate with a few leucocytes. Cellular infiltration of the septa was seen. Only a very few amniotic scales were found in the alveoli. Diagnosis: atelectasis; bronchopneumonia.

CASE 12.—Areas of atelectasis alternated with well distended alveoli. The latter were plugged up with abundant amniotic material. There were only occasional cells within the alveoli. Diagnosis: aspiration; atelectasis.

CASE 13.—The alveoli were collapsed. The capillaries and the larger blood vessels were engorged. There was no amniotic matter in the alveoli. Diagnosis: atelectasis.

CASE 14.—Atelectatic areas alternated with distended alveoli. The latter contained albuminous coagulated material. Diagnosis: atelectasis; edema of lungs.

CASE 15.—The alveoli were mostly collapsed. The septa showed cellular infiltration with polymorphonuclear leucocytes. A few amniotic scales were found only in the larger alveoli. Diagnosis: atelectasis; incipient pneumonia.

CASE 16.—The lung was almost completely aerated. Abundant amount of amniotic matter was present in the alveoli. There were a few leucocytes in the septa but no exudate in the alveoli. Diagnosis: aspiration.

CASE 17.—Parts of the lung were similar to the previous one. In other parts however, there was extensive infiltration of the septa and the alveoli were filled with cellular exudate. The bronchi contained much pus and desquamated cells. Diagnosis: aspiration; focal bronchopneumonia.

Summarizing our findings we observed that out of 39 full-term stillborns and early deceased children evidences of pneumonia were obtained

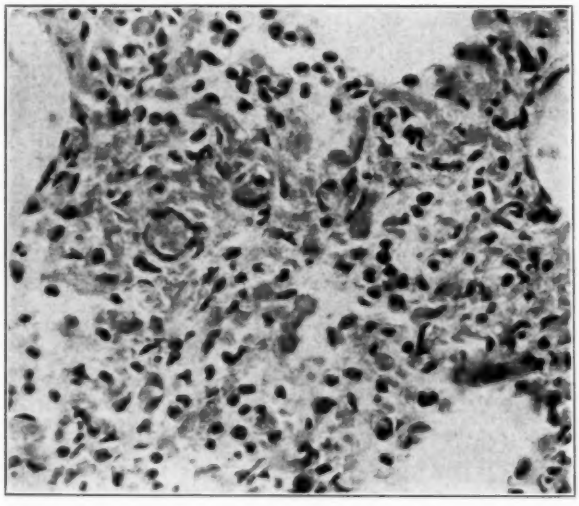

Fig. 4.—Interstitial inflammation in a case of congenital pneumonia. Broadened interalveolar septa infiltrated with polynuclear and mononuclear leucocytes.

in 12. Nine were diagnosed *only* by the microscopic examination, an incidence of 52 per cent, high enough to indicate the absolute advisability of examining histologically the lungs of every stillborn and early deceased newborn where the lack of gross autopsy findings leave the death unexplained.

Amniotic matter, such as scales, fat and lanugo were found in various amounts in the bronchi and alveoli of 13 cases, that is, an incidence of 76 per cent. These 13 cases included those 9 cases that showed evidences of pneumonia and 4 other cases where no signs of inflammation could be found. The fact that no case of pneumonia was observed which did not show the presence of aspiration material supports the belief that aspiration is, if not the sole, at least the most important etiologic factor in the development of congenital pneumonia. Farber and Sweet have

shown the relation of aspiration of amniotic sac contents to intrauterine asphyxia and report the presence of amniotic matter in 88 per cent of their cases.

As to the pathogenesis of congenital pneumonia, Bochenski, Groebel, Lubarsch, Viti, Durante, Menetrier and Touraine believe that the infection is a hematogenous one. Despite the fact that a diseased condition of the placenta or any lesion of the membrane could not be found by them, they base their theory on the fact that the mother has suffered shortly before or during labor from an infectious disease. Although bacteria may travel through the placenta (Raineri) and cases are on record, as for instance that of O'Connor's, where a child died thirty hours after its birth from streptococcus pneumonia, whose mother was found to be suffering from sinus disease. Although the possibility of a

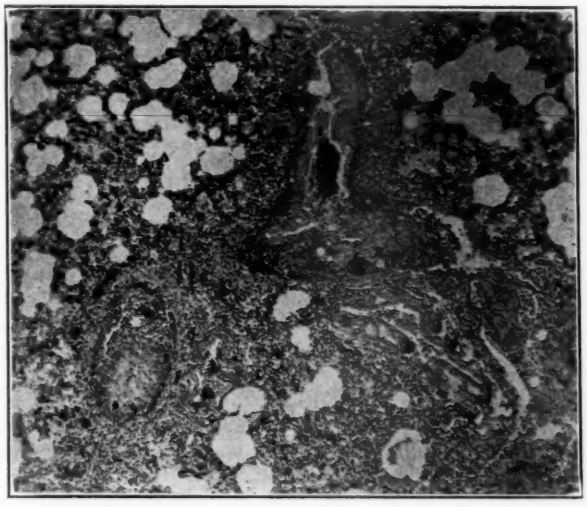

Fig. 5.—Bronchitis, peribronchial, and perivascular distribution of the inflammatory process in a case of congenital pneumonia.

blood stream infection cannot be denied as in congenital syphilis, yet from the definite pathologic evidences as shown above, and will be discussed further in this article, we believe that intrauterine pneumonia as a rule is not brought about by an infection through the circulation.

In those cases that are reported in the literature where the mother has been suffering with bronchopneumonia or lobar pneumonia and on autopsy of the child a similar condition was found, the assumption that the child received an aerogenous infection immediately after birth can be entertained.

According to Murit, the pneumonia toxins of the mother, upon reaching the fetal lungs through the placenta, may set up a susceptibility to bacterial invasion and of late Lauche explains the development of the unspecific congenital pneumonias on an allergic basis.

The majority of authors however, as Silberman, Tingle, Lehman, Johnson, O'Connor, Hook and Katz, et al., favor the belief that seems also to us not only as the more plausible but also as the verified pathogenic cause. Namely, that most pneumonias in the newborn, develop intrauterine and are of bronchogenic origin.

For a long time the question was undecided as to whether the fetus performs any intrauterine breathing or not. Ahlfeld was the first to observe this occurrence with the aid of graphic tracings and Walz asserts that intrauterine breathing is a necessary aid to the fetal circulation. But Schmitt does not consider that the suction caused by the expanding and contracting thorax is of any proved assistance at all to the venous circulation in the adult, and it therefore seems of still less importance in the fetus. Present day opinion is, that under normal and healthy conditions intrauterine breathing of the fetus does not occur. However, under abnormal circumstances it may manifest some irregular breathing and from that, aspiration will result unavoidably. Obstetricians are familiar with the short and snappy inspiration that the child will sometimes draw on the intrauterine manipulation of the accoucheur's hand.

According to Bartholomew, Dyroff and others, the same factor that elicits the first inspiration and lusty cry in the delivered healthy baby, may cause if present under abnormal conditions, untimely breathing. This factor is the CO_2 accumulation in the fetal circulation. An excess of CO_2 in the child's blood may result from reasons originating in the mother, placenta or cord. Circulatory disturbances of the mother, due to pneumonia, decompensated heart lesions, tuberculosis, anemia, drugs, anesthetics as well as tetanic contractions of the uterus, premature separation of the placenta, placenta previa, compression of a low implanted placenta by the baby's head, infarct of the placenta, knots of or pressure on the cord and loops around the neck, all may raise the level of the CO_2 above normal and become a stimulant to the respiratory center. This physiologic action of the CO_2 gains practical therapeutic application in Henderson's treatment of asphyxia with "Carbogen," which is an aeriform mixture of 7 per cent CO_2 to 93 per cent oxygen.

In our own 12 cases of congenital pneumonia we found the mother suffering from mitral stenosis and asthma in 2 cases, the child born in breech presentation with the application of forceps to the aftercoming head in 3 cases, and in another 3 cases the labor was exceedingly prolonged, having from forty to sixty hours in the first and from twenty to thirty hours in the second stage. In one case the child was born in asphyxia livida and in the 3 remaining cases the labor as well as the delivery was normal and uneventful.

Beside the fact that the child in utero may aspirate due to lack of oxygen, two pathologic findings are irrefutable proofs that congenital

pneumonia is bronchogenic in origin. One is that aspirated matter, composed of hornified epithelial cells, fat, lanugo, meconium particles, is found in the bronchi and bronchioli as well as in the alveoli. The second is that these alveoli are no longer collapsed as in an atelectatic state but are opened up just in such a manner as the air pressure unfolds them in the course of breathing. It would be difficult to imagine that a hematogenous transmission of bacteria into an atelectatic lung should cause the evolution of the alveoli in the aforesaid manner.

The larger bronchi as a rule rarely show any congestion or inflammation with mucopurulent discharge. The reason for this is probably, that the pathogenic agent, which besides being a chemical rather than a bacterial irritant, reaches the lung tissue suddenly, passing through the bronchi rapidly.

If signs of pneumonia are found in the stillborn, its intrauterine development is unquestionable and the designation of "congenital" is warranted. The same is vindicated if the pneumonia in an early deceased child is found in such advanced stage of its progress that it is incompatible to the length of time the child has lived. As for example, in Cases 2, 4, 17, where the span of life was from four to seven hours respectively, yet the microscopic report showed the inflammatory process of undoubtedly longer duration.

Hook and Katz term those pneumonias that are found in the stillborn as congenital pneumonia. Those that are found in the early deceased children and show findings of amniotic or birth canal matter they call aspiration pneumonias. They classify them in this manner in order to differentiate them from other aseptic pneumonias that develop from other reasons such as, infected umbilical cord, faulty respiration due to cerebral trauma or food aspiration caused by dyspeptic disorders. However, we differ with the designation of aspiration pneumonia in the case of the early deceased child whose cause of death has been pneumonia with findings of amniotic fluid. We feel these pneumonias too were undoubtedly contracted intrauterine and therefore should also be termed congenital pneumonias.

From a differential diagnostic point of view, pneumonia alba is not easily mistaken with congenital pneumonia. In the latter no chronic inflammatory changes of the septa, connective tissue proliferation or granulation tissue with chronic cellular infiltration of the vessels can be seen, nor can any spirochetes be found.

We are not ready to answer the question with absolute assurance as to whether congenital pneumonia is the cause of death in the stillborn, because it cannot be determined to what degree the breathing surface of the lung can be impaired without becoming insufficient to maintain life, yet we feel that if it is the only ascertainable pathologic finding it shall be accepted as the cause of fatality.

The clinical diagnosis of congenital pneumonia in the stillborn is of course impossible. In short lived children either no constitutional reaction is found or symptoms of a more or less pronounced bronchopneumonia are present. However, a presumptive diagnosis can be made if in conjunction with the auscultation and percussion findings, the history reveals such birth complications as have been enumerated previously and especially so, if the child was born in asphyxia livida or showed from the beginning embarrassed, irregular or weak respiration.

The occurrence of congenital pneumonia in normal cases of childbirth, as in three instances of our series, where the labor was short and the delivery was void of any complications whatsoever, shall be noteworthy for both the obstetrician and to executives of forensic medicine. A thorough microscopic examination of the lungs may often absolve the obstetrician from responsibility in the stillbirth or early death of the infant and may also avoid serious errors of indictment in suspected infanticides.

CONCLUSIONS

1. Congenital pneumonia was found in one-half of the cases of stillborn and newborn children that showed no other cause of fatality.

2. Three-quarters of the cases showed the presence of aspiration matter in the lung tissue. Because of the fact that such aspiration material was always present in the cases of congenital pneumonia, it is assumed that aspiration is responsible for the inflammation and together with atelectasis may be the cause of death.

3. Congenital pneumonia is bronchogenic in the vast majority of cases.

4. The advisability of a microscopic examination of the lungs of stillborn and early deceased children is stressed.

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DISCUSSION

DR. CHARLES A. WEYMULLER.—Every baby who has cyanosis must be suspected of having congenital pneumonia. Obviously intracranial hemorrhage and suprarenal hemorrhage must be considered as well. In an extensive clinical study of this type of lesion we have been able to collect about 60 instances. The only possible means of diagnosing them has been by the x-ray. Clinically, even though there are definite x-ray findings, no physical findings can be elicited. The collapse-syndrome found in the early days of life is no different in intracranial hemorrhage, intrathoracic lesions and suprarenal hemorrhage, or so slightly different that it is impossible to make a diagnosis. The question always arises, when there are abnormal shadows in the x-ray film, as to whether they are due definitely to an inflammatory lesion of this type, or whether perhaps they are due to aspiration of noninfectious material. It is entirely impossible, if the patient lives, to know whether that was true or not. Generally, we suspect that babies who have an intrauterine pneumonia will show a diffuse peribronchial density through the lung field, instead of the massive consolidations that are present in the so-called bronchial plug of atelectasis type.

DR. JOSEPH KALDOR.—In regard to Farber's and Sweet's studies I desire to say that in their paper they simply show the relationship and find an association between atelectasis and aspiration. Furthermore, they have developed a certain staining technic with which they not only can show up these hornified epithelial cells, fat and lanugo in the alveoli, but also the vernix caseosa as a vernix membrane.

SUBACUTE BACTERIAL ENDOCARDITIS AS A COMPLICATION OF PREGNANCY

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THE infrequency of subacute bacterial endocarditis as a complication of pregnancy prompts the report of two cases occurring on the Obstetrical service of the University Hospital during the past five years.

Subacute bacterial endocarditis was first recognized as a clinical entity in 1852. Osler,[10] in his Gulstonian Lectures based on a series of two hundred cases, credits W. S. Kirkes as the first to give an unmistakable account of the disease, while he himself first organized and gave a comprehensive picture of the entity. Subsequently, an enormous volume of writings on the subject has emerged from many pens.

Blumer[2] notes that subacute bacterial endocarditis usually occurs in the third decade of life in patients who have had antecedent diseases producing heart damage, and seems to select those having well compensated valvular lesions. Its onset is insidious and the course prolonged, hence the name coined by Schottmüller in 1910, "Endocarditis Lenta." Although a streptococcus, usually viridans, is the infecting organism in an overwhelming majority of cases (95 per cent), a small number are caused by other organisms, chiefly the influenza bacillus. The outcome is almost always fatal in three to eight months. Osler emphasized the cardinal diagnostic features: fever, the existence of an old valve lesion, embolic phenomena, and positive blood cultures. These criteria are excellent, and with the possible exception of the history of an old valve lesion, should all be present to justify a diagnosis.

In the light of these criteria most of the cases reported as complicating pregnancy are readily determined to be endocarditides of other types. Walser[11] gave an excel-

lent review of the literature in 1928 from the standpoint of pregnancy complication, added two cases, and said, "The only definitely positive case found was the case reported by Findley in which the causative organism was isolated. . . . ." A review of some of the supposed cases, LeGendre,[8] Burgess,[1] Norton,[9] Caussade and LeRasle,[3] shows them to be atypical. Osler's[10] four cases are not given in sufficient detail to enable one to judge of their true identity, and even Croom's[4] case, though rather convincing from the standpoint of the anamnesis, is lacking in two particulars; proof of the causative organism, and of embolic phenomena: Kobacker[7] and Reid[12] reported undisputed cases in 1930. The available and definite reports of subacute bacterial endocarditis accompanying pregnancy are: Findley[5] 1921, Walser[11] 1928, Reid[12] 1930, and Kobacker[7] 1930. To these are added the following two.

CASE REPORTS

CASE 1.—White primigravida, aged twenty-one, was admitted to the University Hospital November 20, 1930, in the sixth lunar month of pregnancy, apparently in good health. The last menstrual period occurred during the first week of May, 1930. The patient gave a history of scarlet fever at the age of five, and at fourteen years she had lobar pneumonia with empyema followed by drainage and extremely painful swelling of the knee, ankle, wrist, and elbow joints, necessitating a total period of six weeks' bed rest. Three weeks after getting up she developed a cough, dependent edema, and became short of breath. Following recovery from this episode she remained well until the present time.

Physical Examination.—The patient was a well developed and nourished woman, normal except for a slightly enlarged thyroid, an operative scar on the right side of the thorax, and a markedly enlarged heart with the left border 15 cm. from the midsternal line. There was a double aortic murmur and the apex first sound had a slapping quality with a suggestion of presystolic roughening. There was no edema of the extremities, moisture in the lungs, or any other sign of cardiac decompensation.

Antepartum Course.—There was a daily remittent fever rising each evening as high as 100° to 102° F. Blood cultures taken December 13, 16, 22, and 26 showed nonhemolytic streptococci which grew both aerobically and anaerobically. A catheterized specimen of urine on January 6, 1931, showed chemical and microscopic blood, and small petechiae were found in the lower left conjunctiva and on the right palmar surface.

Labor.—On January 20, two months after admission, she went into labor spontaneously and after an eighteen hour first stage, controlled by energetic administration of morphine and scopolamine, was delivered by breech extraction of a 2558 gram normal female child.

Postpartum Course.—Immediately following delivery the patient's temperature rose to 102° F. and during the rest of her postpartum course fluctuated between 102° and 103° F. During the second week after delivery the spleen became palpable and tender and more petechiae were found in the conjunctivae. Examination on the seventeenth postpartum day showed normal involution of the pelvic structures despite the febrile puerperium. The uterus was about twice the size of the nonpregnant organ, and the adnexa and the parametria were free. Twenty-one days after delivery the patient was transferred to the medical service where her course was a continuation of the immediate postpartum period. Blood culture again showed a nonhemolytic streptococcus. She developed an abscess of the left labium majus in the region of Bartholin's gland and was returned to our service for its drainage. She was discharged March 4, 1931.

Follow-Up.—A letter from the patient's home physician said, ". . . . After her return from the hospital I did not see M—— P—— until April 24. At this time she was suffering from an extreme degree of cardiac failure. . . . . On May first

I saw her again on account of a small painful infarct of the left forefinger. Soon after this there were multiple infarcts, the most serious being into the right kidney. . . . . The kidney was markedly enlarged and painful, and the urine was loaded with blood and casts of all descriptions.'' The patient's father wrote that she died on May 18, 1931, six months after her admission to the hospital.

The baby left the hospital in good condition and when last heard of, August 11, 1931, was in good health. No blood cultures were taken.

CASE 2.—A white, twenty-seven-year-old patient was admitted to the University Hospital September 5, 1927, in the ninth lunar month of her fifth pregnancy complaining of malaise, afternoon fever, and sweating for more than four weeks. She had been restless, had lost weight, and had pain in the right side of the abdomen. Her general health had been good, except for measles, parotitis, and tonsilitis some years earlier.

Physical Examination.—The left border of the heart was 12 cm. from the midsternal line, and there was a loud rough systolic murmur at the apex transmitted to the left axilla. The sclerae were definitely yellow.

Antepartum Course.—There was a remittent fever ranging as high as 103° F. A blood culture and a Widal test were negative.

Labor.—On September 11, six days after admission, labor began spontaneously and was terminated after a first stage of six hours by breech extraction. The child was a normal 3006 gram female.

Postpartum Course.—The temperature continued as high as before labor, but the remissions were less marked. Four days after delivery the spleen was palpable and very tender, and there was tenderness over the left kidney region. Another blood culture taken at this time was negative. Pleurisy developed in the left chest and the patient showed a loss of memory. Eight days after delivery the urine became grossly bloody, and chemical and microscopic tests for blood were markedly positive. Two days later the edge of the liver was palpable and tender, and the patient was transferred to the medical service. Blood cultures taken October 12, 17, 18, and 19 showed Streptococcus viridans. On November 1, 1927, fifty-one days after delivery, the patient died.

Autopsy.—November 1, 1927. Heart: The mitral valve had a group of cauliflower, friable vegetations on each leaf. Spleen: This organ was enlarged, weighing 610 gm. There was a recent infarction, 9 cm. at its greatest diameter, in the upper pole and several smaller infarctions, one of which had broken down to form an abscess. Kidneys: The left kidney showed an old depressed scar 3 cm. long, probably representing a healed infarct. Genitalia: completely normal. Streptococcus viridans was grown from the vegetations on the mitral valve, and cultures taken from the heart's blood showed the same organism.

The baby was discharged on the twenty-eighth postpartum day apparently in good condition, and weighing 3524 gm. No blood culture was taken.

COMMENT

Each of these patients had the two most important features of subacute bacterial endocarditis, repeated positive blood cultures, and embolic phenomena. Case 1 satisfies all of Osler's criteria, while Case 2 did not have definite evidence of previous heart damage. She gave a history of tonsilitis, measles, and parotitis, and had a mitral lesion on admission, but we have no certain knowledge that the heart damage existed prior to the onset of her terminal illness.

Curiously, both babies presented by the breech, but this was surely a coincidence. No blood cultures were taken from the infants, so it is im-

possible to add to Walser's[11] observation of placental transmission of the infecting organism. However, they survived and were normal in all respects as long as they were under observation.

The infecting organisms were Streptococcus viridans, and a nonhemolytic streptococcus.

In view of the grave prognosis of subacute bacterial endocarditis, we did not feel justified in Case 1 in interference of any sort, believing that delivery by the most conservative means after full dilatation of the cervix, with plentiful use of morphine and scopolamine during the first stage, offered the best chance for the child without adding appreciably to the mother's risk. We could see no advantage in abortion, believing that the mother's chance for survival would not be improved and that it was justifiable to await a living child.

Delivery did not affect the course of the disease materially, and neither patient developed infection of the uterus or parametria. This absence of involvement of the genital organs in the presence of a known blood stream infection is confirmed by Walser's[11] and Findley's[5] cases. The patient whose case was reported by the latter rallied for two weeks after delivery, dying later in uremia, and neither of Walser's[11] patients developed any evidence of uterine or parametrial involvement. Kobacker's[7] patient was delivered by cesarean section in a successful attempt to obtain a living child. The mother was in a desperate condition and died four days later. At postmortem examination the site of the uterine incision showed "extensive necrosis and infective degenerative changes with resultant loosening of the sutures."

Reid's[12] case is not given in sufficient detail to add materially to these observations. His patient aborted at the fifth month of her sixth pregnancy during the course of a febrile disease from which she died five months later. "Streptococcus viridans was present in the blood cultures both in life and at the necropsy."

CONCLUSIONS

Subacute bacterial endocarditis does not seem to affect the course of pregnancy, labor, and the puerperium materially.

Pregnancy complicated by subacute bacterial endocarditis should be allowed to proceed to normal conclusion because the mother's course is almost certain to terminate fatally, and it is extremely doubtful if sacrifice of the child contributes, even in the smallest way, to her chance of survival.

Delivery by the most conservative means possible after full dilatation of the cervix with plentiful first stage analgesia is the obstetric treatment of choice.

Cesarean section is justified only in the interest of the baby when the mother is in extremis.

The babies seem to do well if they are not too premature at birth.

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HEART-BLOCK IN PREGNANT WOMEN

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In the November, 1931, issue of the American Journal of Obstetrics and Gynecology appeared an article on "Normal Pregnancy in a Patient With Preexisting Complete Heart Block" by R. S. Titus and W. B. Stevens.[1] The authors reported a case of complete heart-block in a pregnant woman and stated they could locate published reports of only four similar cases that had been permitted to go through to full term. The purpose of my communication is to point out five additional reported cases of heart-block, not all of whom had heart-block before pregnancy supervened, and to place on record a case which recently came under my observation.

The first case of complete heart-block complicating pregnancy which was reported in the literature was the one described by H. Freund[2] in 1918. His patient was an octipara who developed Adams-Stokes symptoms one and a half hours after having had a miscarriage. She died suddenly a few hours later with symptoms of complete heart-block. Autopsy revealed both an acute and a chronic endocarditis. The author had observed signs and symptoms of heart-block during the seventh pregnancy, but the patient had no symptoms during the interval between the seventh and the eighth gestations. Freund therefore was of the opinion that pregnancy and labor exercised a detrimental influence on the conduction system of the heart.

The second case was reported by Walz[3] in 1922. A primipara was perfectly well until 1918 when she became ill with influenza and as a consequence of it developed heart trouble. From that time her pulse was very slow, and she had frequent fainting attacks. Not until she became pregnant did she notice any improvement. When first examined by Walz, the patient's radial pulse was 40 per minute, whereas the venous pulsations in the neck were approximately 80 per minute. Pregnancy was uneventful and labor was easy and spontaneous. The first stage lasted five hours and the second only thirty-five minutes. The child weighed 3150 gm. (6 pounds 15 ounces). During the puerperium the pulse never rose above 40 per minute. The patient left the hospital nine days after delivery. Electrocardiograms were taken and showed a complete heart-block.

Another case not included in Titus and Williams' paper, (most likely because their paper was written before this case appeared in print and because the heart-block did not manifest itself until after labor) was that reported by P. Herskovics[4] in April, 1931. A primipara had had polyarthritis at the age of fifteen, and since then had suffered with symptoms referable to the heart. During her pregnancy however, she had no cardiac symptoms and her pulse was 84 per minute. She had a spontaneous labor and delivered a child weighing 2700 gm. (5 pounds 15 ounces). Fifteen minutes later the placenta was expelled. Twenty-five minutes afterwards the patient suddenly cried out, became pale, manifested epileptiform contractions of both arms and then became cyanotic. The pulse varied between 13 and 15 per minute

and in spite of all medication and mechanical efforts the patient died. At autopsy the only abnormalities found were in the heart. The heart muscle and the valves were normal but in the region of the Aschoff-Tawara nodes, at the opening of the coronary sinus was a small cavity from which two drops of thick, yellowish, purulent secretion could be expressed. The probable etiology was a bacterial-metastatic or a rheumatic infection. This produced no disturbance during pregnancy but labor had such a deleterious effect on it that it caused fatal heart-block.

Two more cases of complete heart-block were reported by McIlroy and Rendel[9] in an extensive paper on "The Problem of the Damaged Heart in Obstetrical Practise." The description of these patients is as follows: "Complete heart-block. Two patients, one suffering from congenital heart disease and left bundle-branch block and the other from myocardial degeneration. Both these patients did very well, the first one not showing any signs of failure. The second patient had slight disability during her first pregnancy, but has just gone through another with very few symptoms and has had twins. This patient however, had three Stokes-Adams attacks immediately after delivery."

Among the eleven cases reported in the literature (Freund, Walz, Jeannin and Clere,[5] Laubry,[6] Dressler, 2,[7] Herrmann and King,[8] Herskovics, Titus and Stevens and McIlroy and Rendel, 2, there were two deaths (Freund and Herskovics).

AUTHOR'S CASE REPORT

Mrs. J. K., a primipara, aged thirty-five years, had a negative family and personal history except that she knew she had an unusually slow pulse rate ranging around 50 per minute. In spite of being married seven years, this was her first pregnancy. Her last menses began July 20, 1930, and conception was believed to have occurred on July 27. Quickening was observed December 10, 1930. When first seen by Dr. W. E. Brown of Cedar Rapids, Iowa, the patient's pulse was only 50 per minute. Because of this he referred her to Dr. B. F. Wolverton who, from physical examination and electrocardiographic studies, made a diagnosis of complete heart-block associated with rheumatic heart disease and mitral insufficiency. The electrocardiograms are shown in Fig. 1. Because of the repeated fainting attacks and periods of marked bradycardia the patient was admitted to the St. Luke's Methodist Hospital in Cedar Rapids on March 24, 1931. On admission the heart action was irregular. The apex and radial pulse rate averaged about 48 beats per minute whereas the jugular pulse rate was 90 per minute. The left border of the heart was 4½ inches to the left of the midsternal line. The apex was 4 inches to the left of the midsternal line in the fifth intercostal space. The right border was one inch to the right of the midsternal line. A diastolic murmur was heard at the apex and was transmitted to the axilla. The blood pressure was 110 systolic and 60 diastolic. The lungs were clear. The liver and spleen were not palpable. The uterus was the size of an eight months' pregnancy, the presentation was O.L.A. and the fetal heart rate varied between 140 and 160 per minute. The urine was normal except for the presence of acetone. The pelvic measurements were normal.

After admission to the hospital, the patient's condition became worse. She fainted more frequently, she was frightened a great deal of the time, and she was restless, dizzy, and weak. The pulse varied between 32 and 40 but the auricular rate remained around 80. An electrocardiogram showed complete dissociation. The blood pressure gradually rose. On April 7, the systolic pressure was 160 and the diastolic pressure 70 and on April 11, the systolic was 180 and the diastolic 80. There was no evidence of aortic insufficiency. Another electrocardiogram taken on April 9, when the blood pressure was 170 systolic and 76 diastolic revealed no changes. The QRS wave in both tracings was 10 mm. Lead I showed no axis deviation and no conduction deficit in the bundle branches or the ventricles. At one time the pulse went as low as 18 per minute. The medication consisted of digifolin, barium chloride

and adrenalin. On April 13 I was called to Cedar Rapids by Dr. Brown to perform a cesarean section. At the beginning of the operation the pulse was 52 and it remained almost the same throughout the operation. The blood pressure at the beginning was 150/80 and it varied between 142/80 and 180/84. I performed a transperitoneal, cervical cesarean section (laparotrachelotomy) and used local anesthesia not only for the cesarean section but also for the sterilization operation, which consisted of crushing and doubly ligating the tubes according to the Madlener procedure. The baby which weighed 2310 gm. (5 pounds 1 ounce) was in excellent condition. Convalescence was entirely uneventful. The patient was permitted to sit up in a chair on the twelfth day after operation, and she and her baby left the hospital in good condition on the fifteenth day. During the puerperium the pulse varied between 29 and 43 beats per minute and the blood pressure was normal. The highest temperature was 100.8° F. and this occurred on the third postoperative day.

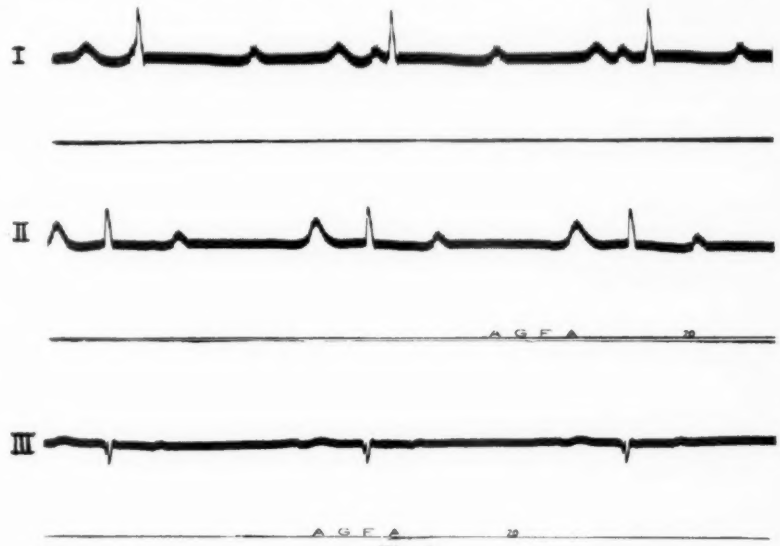

Fig. 1.

COMMENT

Heart-block complicating pregnancy is a rare and serious condition. Of the twelve cases reported in the literature including the case herein described, there were two fatalities, a death rate of almost 17 per cent. Undoubtedly many more cases of heart-block in pregnancy have been observed but have not been reported. As Titus and Williams point out, heart block during pregnancy is extremely rare in women who had the block before pregnancy supervened. Probably one of the reasons for this is that heart-block usually occurs in individuals over forty years of age. On the other hand, it is not very uncommon to observe heart-block during pregnancy, labor, or the puerperium as a temporary condition in women who do not have the heart-block at any other time. In every case of heart-block complicating pregnancy, labor, or the puerperium, a cardiologist should be called in consultation by the obstetrician. In patients with perfect compensation and without untoward symptoms delivery through the natural passages should yield

good results for both mother and child. The second stage should be shortened in primiparas by means of a low forceps operation under direct infiltration anesthesia of the perineum and vagina. In women with evidences of decompensation the low cervical cesarean section under local anesthesia before labor sets in is the safest procedure.

I wish to thank Dr. W. E. Brown for the details concerning the case and also for the excellent care he gave the patient after operation.

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SOME UROLOGIC COMPLICATIONS IN THE FEMALE*

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THE interest that gynecologists in recent years have taken in urology makes it opportune to bring up for discussion a few instances where the results of modern investigations help to supplant routine treatment with rational therapy. Formerly and to a certain extent even today under the term incontinence was applied to clinical manifestations of entirely different origin. Now we know how to differentiate pollakuria and imperative urinary frequency based on inflammatory processes of urination, from true incontinence based on insufficiency of the sphincter muscle. I am not going to discuss the extreme cases of complete incontinence where on account of total destruction of the sphincter transplantation of fasciae and muscles has to be resorted to, but will confine myself to those cases of relative incontinence in which any increase of the abdominal pressure leads to dribbling or complete evacuation of the bladder.

In juvenile individuals resistance gymnastics practiced with a straight urethral sound as a rule is followed by good results. The resulting hyperplasia of the sphincter muscle may be evidenced by digital palpation, the strengthened sphincter muscle to be felt as a protruding ridge.

In older patients whose reconstructive power is somewhat impaired this procedure may fail. Then we resort to a rather simple endovesical method. Employing an operative or catheterizing cystoscope a fine electrode is introduced into the bladder and running a cutting current a few superficial incisions are made into the mucosa, these incisions extending about 1 cm. into the bladder and reaching just as far into the urethra. We use about the same technic as employed in the linear cervical incisions for endocervicitis. It is advisable to establish these incisions in the upper half

*Read at a meeting of the Chicago Gynecological Society, March 18, 1932.

of the so-called vesical neck and not in the vesical trigone, in order to avoid unpleasant after effects. If the first seance should not prove successful, the procedure may be repeated. Local anesthesia with a 10 per cent novocain or a 4 per cent antipyrin solution makes this method absolutely painless.

Strictures of the female urethra although given more attention than formerly, nevertheless are quite often overlooked because the fact is lost sight of that their presence, location and extent may with certainty only be diagnosed with the help of an olive tipped sound. In this connection I would like to call attention to a complication which is rather frequent and if overlooked may cause pronounced inconvenience if a certain routine treatment is administered. It is common practice to follow dilatation of the urethra with instillation of concentrated silver salt solutions in order to alleviate the symptoms of a supposed cystitis. In fact in a great many instances one finds concomitant with stricture, a retrostrictural edema of the vesical trigone. The trigonal mucosa appears to be whitish and fluffed, imitating the appearance of absorbent cotton. Such a vesical lining is rather vulnerable and reacts very unfavorably to any caustic. Systematic dilatation of the urethra as a rule suffices to restore normal circulation and epithelialization. In stubborn cases medical diathermy is very helpful in restoring normal conditions.

Gonorrheal urethritis in the female quite often subsides spontaneously if reinfection is avoided, but occasionally it may assume a chronic character, thus not only being bothersome but also furnishing a fruitful source of infection for other pelvic organs. Whenever one encounters a chronic urethritis with copious discharge urethroscopic examination should be undertaken. In such instances one finds disseminated granulations of the urethral mucosa generally located over the opening of the urethral glands. Scrapings of these granulations demonstrate a meshy structure whose cavities are filled with gonococci, explaining the stubborn character of urethritis of this kind. Electric destruction through an urethroscope furnishes prompt and lasting relief.

Another source of great annoyance are varicose veins in the vesical mucosa. Sizeable varicosities may not only be productive of submucous and open hemorrhages but in many instances cause intolerable itching sensations within the bladder. This symptom may be explained by the slowing up of the local circulation and also by the loss of the epithelium over the venous nodules similar to the sensations around surface varicosities. Formerly these varicosities were not amenable to endoscopic therapy and in extreme cases one had to resort to cystotomy and excision or destruction of the dilated veins with the actual cautery, either one an operation of importance. Nowadays we are in a position to obliterate these nodules by applying the high frequency current through a cystoscope, a simple and safe procedure the same as the destruction of a benign papilloma. Local or sacral anesthesia guarantees a painless procedure.

Omission of cystoscopic and functional examination may in another instance be responsible for a therapeutic error. It is a rather common occurrence that especially in young females during the course of a toxic or bacterial nephritis, submucous hemorrhagic patches are established in the vesical mucosa, which are apt to produce various disagreeable symptoms.

If these conditions are not recognized and, as is so often the case, urotropin or similar drugs are administered, the whole situation is aggravated. In some individuals such medication is apt to produce vesical hemorrhages though nephritis may not be coexistent. But if such patches are already present this medication accentuates the pathology and pronounced hematuria with concomitant extensive loss of epithelium is apt to occur. In all instances of this kind antinephritic régime has to be instituted and any local treatment of the bladder has to be omitted.

In doing prolapse operations or hysterectomies, the operator may miss the proper cleavage and open the bladder wall while freeing the viscus from its attachment to the portio. The resulting interference with the circulation produce then areas of epithelial desquamation in the base of the bladder, causing disagreeable symptoms. If without cystoscopic control the usual diagnosis of postoperative cystitis is made and instillations with irritating solutions are administered the syndrome is aggravated. The epithelialization of these defects takes place spontaneously as soon as proper circulation is reestablished. Mild diathermic treatments are apt to accelerate this restoration. It seems that in prolapse operations the detachment of the bladder not only from the cervical junction but also laterally from the broad ligaments is of importance. In order to dispose of the retention in an extensive cystocele it seems to be necessary to bring the entire bladder under the influence of abdominal pressure. If however the lateral detachment of the bladder is neglected, a double saddle bag formation of the bladder will result. In this way urinary retention with all its undesirable sequelae will be the result.

The troublesome occurrence of pyelitis in the female has become somewhat mitigated, by the introduction of intravenous urography. This enables us to visualize the urinary ways without the vitiation by artefacts produced by retrograde pyelography. Systematic revision of the results obtained by pelvic lavage in pyelitis lead some observers to the conviction that this method is only indicated and successful in the instances of a dilated pelvis. Visualizing the renal pelvis by retrograde pyelography does not enable us with certainty to differentiate a dilated pelvis from a dilatable one. In the latter instance repeated instrumentation is apt to produce irritation and aggravation of the symptoms. This is especially true in pregnant women.

Another item may be mentioned which though not strictly urologic in the usual sense in medicine, is the occurrence of certain nephrotic conditions. The latter constitute most of the renal disturbances in pregnant women. As a rule they do not constitute an indication for interruption of

pregnancy and usually will subside under proper régime after delivery. The term nephritis is used for capillary toxicosis of the kidney and its sequelae, while the pathologic renal substratum in nephrosis is degeneration of the tubular epithelium without involvement of the glomeruli. Nephritic conditions are characterized by the retention of the organic metabolic end products, nephrosis is accompanied by disturbances of the lipoid economy of the body and the retention is confined to the inorganic end products. Nephritic edema contains proteins and no chlorides, nephrotic edema is characterized by high chloride contents without proteins. In gynecologic operations nephrosis may assume great importance. For some as yet unaccountable reasons nephrotic patients are very prone toward the establishment of pneumococcus infections. Perfectly clean laparotomies may in such instances lead to death on account of postoperative pneumococcus peritonitis. Timely diagnosis and appropriate treatment may prevent such infaust accidents.

THE USE OF ADRENALIN IN THE TREATMENT OF ACUTE INVERSION OF THE PUERPERAL UTERUS, WITH REPORT OF A CASE

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THE work of Huntington, Irving and Kellogg (1928) and the recent paper of Irving and Kellogg (1931) upon the reposition of the acutely inverted puerperal uterus by laparotomy, has again called attention to this serious complication of labor.

Because of the rarity and the high mortality of the condition, as shown in Findley's (1929) recent paper, it would seem justifiable, in spite of the fact that a large series of cases is not available from which one could draw definite conclusions, to report any adjuncts to the accepted method of treatment.

It is admitted that the greatest immediate danger in the treatment of the acutely inverted puerperal uterus lies in attempts at replacement through a contracted cervix, in the presence of shock that almost always accompanies the condition. The generally accepted procedure is to control bleeding, replace the uterus in the vagina and treat shock by all available means, with the idea that later the replacement may be carried out with minimal danger to the patient.

It has been pointed out, however, by Findley and others that this delay may result in contraction of the cervix and subsequently defeat all efforts at replacement. The contracted cervix, then, presents a barrier to either manual or operative replacement. The treatment must be directed toward an alleviation of this spasm of the cervix when the patient is in condition to withstand the trauma of replacement.

Rucker (1925, 1927, 1931) has described the effect of adrenalin upon the human uterus and has shown that 5 minim doses of 1-1000 solution caused a cessation of labor pains for a period of nine to thirty minutes in 16 out of 20 patients. In addition, he had used adrenalin successfully in the treatment of contraction ring dystocia and in difficult deliveries demanding uterine relaxation.

Rudolph and Ivy (1930) have demonstrated that adrenalin injected into dogs in labor, produced a temporary relaxation of the uterus which lasted for three to ten minutes. They also found that it inhibited the contractions produced by ergotamine tartrate and pituitrin.

Ivy, Hartman and Koff (1931) in experimenting with the ante- and postpartum uterus of the monkey found that the injection of adrenalin produced a single uterine contraction which was followed by a relaxation period of five minutes or longer. They confirmed the work of Rudolph and Ivy as to the effect of adrenalin upon the contractions induced by pituitrin.

With the foregoing in mind the following case report is submitted:

Mrs. E. O., aged twenty-five, para ii, gravida iii, was admitted to the obstetric service of the General Hospital at 8:00 A.M., in early first stage labor. The cervix was about 2 cm. dilated and the membranes had ruptured before admission.

Physical examination revealed no abnormalities. The pelvic measurements were adequate. The position was O.L.A. Pains were moderate but continued with increasing intensity and duration until 9:00 P.M. when she went into second stage labor. At 11:42 P.M. she was delivered of a normal living child. There was minimal bleeding after the second stage which was controlled by gentle massage of the uterus.

At 12:05 A.M. there was a sudden hemorrhage in which approximately 1500 c.c. of blood were lost. An attempt was made to massage the uterus to contraction to permit Credé expression when it was noted that the placenta, membranes, and uterus were at the vaginal outlet. The patient went into shock as her blood pressure dropped to 80 systolic. No diastolic reading could be obtained. Her pulse increased to 160 and was hardly perceptible. The placenta and membranes had to be separated in order to replace the uterus into the vagina. At this time the cervix was found to be contracted down to about 2 cm. in diameter. The patient was quickly placed in Trendelenburg position and pituitrin and caffeine sodium benzoate were given. External heat was applied. The bleeding at this time had stopped; 1500 c.c. of saline were given intravenously which raised the blood pressure to 110/60. The pulse rate lowered to 140 and was of fair quality.

The patient was transfused with 550 c.c. of whole blood. The blood pressure rose until at 1:00 P.M. it was 138/96. The pulse had slowed to 100. Her condition had greatly improved.

At 1:00 P.M., thirteen hours after the inversion, the patient was surgically prepared for manual replacement of the uterus. Atropine sulphate gr. 1/150 was given preparatory to gas-ether anesthesia. She was catheterized. Five minutes before the vagina was entered ½ c.c. of adrenalin was given intramuscularly. The blood pressure rose to 140/88, the pulse increased to 120. Vaginal examination showed the uterus to be firmly contracted and the cervical ring not more than 2 cm. dilated. It had the consistency of cartilage. Pressure in the sulcus gave little hope of reposition. Steady pressure was made against the inverted fundus with closed fist and within one minute (six minutes after the adrenalin was given), it began to soften on its posterior surface. The cervix relaxed to about 4 cm. in diameter. At this time (1:25 P.M.) an additional ½ c.c. of adrenalin was given. The blood pressure remained at 140/88 and the pulse rate at 120. Within one minute the cervix relaxed enough to admit the closed fist and without further difficulty the uterus was completely replaced. An intrauterine pack was placed by hand. The blood loss during the operation was not more than 150 c.c.

Immediate transfusion of 450 c.c. of whole blood was given. The pack was removed in twelve hours. During the puerperium the temperature rose to 100.2° on the second, third, and fourth days. The patient was discharged from the hospital on her sixteenth postpartum day with a well involuted uterus and in good general condition.

SUMMARY AND CONCLUSIONS

The intramuscular injection of adrenalin in this case of acute inversion of the puerperal uterus seems to have been effective in producing relaxation of the uterus and cervix and to have greatly facilitated manual replacement. There is little doubt of its value in protecting the patient from further shock during operation.

It is suggested that adrenalin is a valuable adjunct in the reposition of the acutely inverted puerperal uterus by either manual or operative method.

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A CASE OF LARYNGEAL DIPHTHERIA COMPLICATING THE PUERPERIUM

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FREQUENT mention is made in the literature of puerperal diphtheria, diphtheritic patches being found upon the denuded portions of the vulva and vagina. These are usually a primary genital infection and texts refer to them as sometimes being secondary to diphtheria of the throat. However, a search of the literature for cases of pharyngeal or laryngeal diphtheria complicating the puerperium reveals infrequent mention of the same.

Steen in 1900 reported a case of a woman aged thirty-three well advanced in pregnancy who had a sore throat and nasal discharge. The next day she had a slight membrane on her right tonsil, no pyrexia, and no enlarged glands. Her pulse rate was accelerated and a bacteriologic examination showed the Klebs-Loeffler bacillus. She was given 1500 units of antitoxin and the next day delivered a full-term infant. When the child was four days old it developed difficult nasal breathing and the next day, membrane on its right tonsil. The child was given a total of 1350 units of antitoxin and recovered.

E. Casavecchia in 1901 reported a case of a gravida ii, para ii, twenty-four years of age, who in the eighth month of pregnancy was suffering from diphtheritic laryngotracheal bronchitis. She was given Behring's antidiphtheritic serum in 1000 unit doses and after the fifth injection of serum, the patient delivered a living fetus weighing 2500 gm. The serum was repeated three times and the patient recovered.

D. R. Ranson in 1909 reported a case of a pregnant woman contracting diphtheria from her two children, having diphtheritic membrane in her throat. The woman was given 4000 units of antitoxin followed by 3000 in twelve hours. Ten hours after the second injection her child was born and took the breast, although her membrane and fever remained. The child did not contract the disease and the mother recovered.

I am reporting a case of laryngeal diphtheria complicating the puerperium, this case being unusual in that for three days prior to delivery, the patient had a sore throat. There was no membrane visible at the time and after the development of a clinical virulent laryngeal diphtheria, there was still absence of membrane. This sore throat was not accompanied by any increased temperature or pulse rate and when the disease manifested itself clinically about thirty hours after delivery, a diagnosis was immediately made and heroic measures of therapy instituted but without avail.

Mrs. P. O'H., aged forty-two, gravida vii, para vii. First day of last menses March 24, 1931. Her past medical history is not significant except for pyorrhea alveolaris a year ago for which she had all her teeth removed. The patient's mother died of heart disease in late adult life, and otherwise her family history is negative.

During her present pregnancy she had occasional transitory headaches and attacks of dizziness and swelling of her feet and ankles. She had attacks of gas after eating and was bothered by constipation. Her physical examination was essentially negative except for tenderness in the region of her gall bladder, and her blood pressure and urinary examinations were negative throughout her present pregnancy. On December 11, 1931, while making an antepartum visit to the patient's home, she remarked that her two sons, aged eight and ten respectively, were suffering from tonsillitis which had abated but had left them with "sore glands" in their necks. I looked at the boys but found nothing except some enlarged anterior cervical glands, both their throats being clear. The patient was warned at the time to take great care in not exposing herself to any acute infections as she was very close to term.

The patient was admitted to the Montifiore Hospital December 30, 1931, at 12:45 A.M., stating she had had several labor pains. On examining her in the labor room she remarked that three days ago her maid had a very sore throat and she helped out by doing her own housework. That same evening her throat became sore and had bothered her ever since. Examination of her throat revealed a slight injection of her pharynx on the left side. Abdominal and rectal examination showed her to be in definite labor and the sore throat was forgotten.

At 2:49 A.M., the patient delivered spontaneously vertex L.O.A., a male child weighing 3880 gm. There was a small first degree tear of the fourchette. The expulsion of the placenta was Schultze spontaneous and the bleeding was slight. The patient had sodium amytal grains VI during the first stage of labor and ether for her perineal stage. She was returned to bed in good condition.

About twelve hours after delivery the patient's pulse, temperature, and respirations were normal. She was feeling fine except for her sore throat. Examination at this time showed some increased inflammation of the left tonsil with a small pus pocket. Her throat was painted with 10 per cent silver nitrate and a gargle prescribed.

Early the following morning, December 31, 1931, at 12:30 A.M., the patient was awakened by her sore throat which kept her uncomfortable during the whole night. Toward daylight she began to have increased expectoration, difficulty in swallowing, loss of voice, not being able to talk above a whisper, some dyspnea and

difficulty in bringing up thick tenacious mucus which choked her. She also complained of a sticking pain deep in her throat pointing to the region of the cricoid cartilage. At 12:40 P.M., her temperature was 102.8°, pulse 148, and respiration 24, and Dr. Friedman of the Nose and Throat Department was called in to look at her larynx. The indirect laryngoscopic examination showed a swelling of the false cords and an entire absence of any false membrane either in the larynx or throat. We were greatly concerned about the possibility of a laryngeal diphtheria, therefore, a direct smear and culture were taken of the patient's throat, and it was decided that if the smear were to be negative for the diphtheria bacillus we would still give the patient a large dose of antitoxin before waiting for the culture report.

The laboratory examined the direct smear immediately and found B. diphtheriae in large numbers. The patient was immediately given 95000 units of diphtheria antitoxin intramuscularly, was removed from the obstetric floor and isolated. The patient was given 500 c.c. of 10 per cent glucose intravenously about one-half hour after the administration of the antitoxin. Since the newborn had been exposed to a seemingly virulent case of diphtheria, he was given a prophylactic dose of 1500 units of antitoxin and also isolated.

Toward evening the patient was becoming more toxic and breathing more difficult. A second examination of the larynx showed such large amount of swelling of the false cords that a view of the true cords was entirely obliterated, and the presence of any false membrane not observed. Dr. J. S. Baird, the Director of the Municipal Contagious Hospital, was called in consultation, and at 10:15 P.M. he intubated the patient because of her marked respiratory difficulty. The intubation immediately relieved her dyspnea and improved her pallor, but she continued to expectorate a now blood stained mucus which was very annoying to her. Morphine and atropine sulphate were given in small repeated doses and the patient spent a very restful night.

The next morning the patient's condition was fair. She was taking liquids in teaspoonful doses and in order to give her more fluid to combat her toxicity 1000 c.c. of 10 per cent glucose was started intravenously. Although the administration was not rapid after 840 c.c., it was stopped because of dyspnea and cyanosis.

Late that afternoon the temperature began to drop, the pulse going up and becoming weak and thready. The patient did not respond to cardiac stimulants, the pallor increased and an acute pulmonary edema supervened. The heart continued to fail and the patient died at 9:00 P.M. The intubation tube was removed postmortem and was found free of obstruction and with a small piece of membrane adhering to its lower pole, the first seen throughout the whole course of the disease. The membrane was cultured in the laboratory and gave a growth of B. diphtheriae.

COMMENT

This case is presented in detail because it has many interesting features. I mentioned the sore throat in the patient's two boys occurring nineteen days before her delivery, and the sore throat in her housemaid three days before delivery, as a possible etiologic factor. Her entire family were therefore immediately cultured, including the housemaid, but with negative results. There was no diphtheria in the neighborhood where the patient lived, and none of her friends or relatives had knowingly been exposed to the disease. Several friends who had visited the patient the night before the onset of the laryngeal symptoms, submitted to culture as well as all the hospital personnel who had contact with the patient, with negative results.

From the reports in the literature the infection of a mature adult woman in the puerperal state with laryngeal or pharyngeal diphtheria, is very rare. This is a chance infection, yet since it does occur, and with such tragic consequences as in this case, it should be kept in mind.

The question of giving the newborn a prophylactic dose of diphtheria antitoxin was quickly decided upon, even though they are thought to inherit a transient congenital immunity. If there was a lack of this immunity in the mother, surely the chances of the infant inheriting such immunity would be obscure. In Steen's case the infant developed diphtheria when four days old, and G. Blechmann and M. Chevalley report two infants contracting the disease from an older infant who was not isolated. They believe that diphtheria is not observed under seven months of age because of relative isolation and not inherited immunity.

Another clinical feature that cannot be overlooked in this case is the cardiac death. I previously mentioned the patient's history of pyorrhea alveolaris and the presence of a mild chronic cholecystitis. These coupled with seven pregnancies that in themselves deplete the cardiac reserve, offer enough undermining of myocardium to make it unable to advantageously withstand the virulent toxin of diphtheria.

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QUININE INSUFFLATION TREATMENT OF TRICHOMONAS VAGINALIS. PRELIMINARY REPORT

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THE fact that Trichomonas vaginitis is a clinical entity and of not infrequent occurrence is not further disputed. Our reason for bringing the subject to attention again is only that the manifold and various treatments have so far proved unsatisfactory. The antiseptics, the dyes, lactic acid, and Lassar's Paste have relieved many cases, cured a few, but the majority come back with a reinfection or recurrence shortly after a menstrual period, or, if treatment is relinquished, after some lapse of time.

It occurred to one of us (J. H. S.) that since the organism is a protozoon, and since quinine is an agent which frequently destroys some of the protozoa, this cinchona alkaloid might be useful in the treatment of such cases.

Case 1.—H. B. P., was seen October 12, 1931, aged twenty-four, married, nullipara, complained of an irritating discharge for some length of time. Trichomonas

four-plus positive. This case was selected because the patient had not been treated before. No cleansing, scrubbing, or antiseptics were used.

The specimen recovered from the patient was studied under the microscope. A small quantity of quinine sulphate powder was mixed with water and allowed to trickle under the cover glass. Immediately the organisms were thrown into a spasm. Several minutes later, the motility and activity of the organisms were seen to diminish and then stopped entirely after a short length of time. Long, narrow crystals, shaped like disorganized cordwood appeared under the microscope, which crystals we learned to recognize as those of quinine.

Quinine sulphate powder, about fifteen grains, was blown into the vagina with a powder blower, and patient asked to report the following day. Next day, specimen taken from the same patient showed many quinine crystals and many dead (non-motile) trichomonads.

Daily insufflations and study of slides showed less and less purulent discharge with disappearance of the trichomonads on the fourth day after the initial treatment.

Patient was not seen for a week during which time she had a four-day menstrual flow. October 22, patient's vagina was perfectly dry, with no discharge, no trichomonads found. After her December 6 menstrual period, slide showed no trichomonads and no discharge. Last seen January 2, 1932, no discharge, no trichomonads, and patient dismissed.

CASE 2.—Mrs. E. W., aged twenty-five, was treated in clinic off and on from March 28, 1927, to October 13, 1931, for neisserian infection. October 13, 1931, she still complained of an irritating vaginal discharge, at which time trichomonads were discovered. Quinine used as in Case 1, October 17, and October 24. October 31, no discharge; November 7, menstruating and quinine used during period. November 14, no discharge and no trichomonads present; November 21, no burning, no itching, no vaginal discharge and no trichomonads. December 5, postmenstrual slide, no treatment, no discharge, no trichomonads. December 12, no trichomonads, no discharge, and no treatment. December 19, no trichomonads and no treatment. January 2, 1932, no discharge, no treatment, and patient dismissed.

CASE 3.—E. S., aged forty-six, was first seen March, 8, 1930, for spotting after coitus, when polypoid endocervicitis was diagnosed. Treated by actual cautery.

February 7, 1931, complained of burning discharge, and trichomonads found. Treated with soap scrub, bichloride douche. Treated at various times to September 19, 1931, with various medicaments, without any improvement. October 3, 1931, Lassar's Paste used. October 10, 1931, trichomonads still present. Quinine insufflation. October 17, 1931, no discharge for the first time in many months and no trichomonads. October 24, 1931, vagina dry, no discharge. Patient not seen since.

CASE 4.—V. B., aged twenty-seven, first entered the out-patient department October 29, 1928, for metrorrhagia and vaginal itching, dating back from a twin delivery in April 1928. The smears showed gram-positive and gram-negative bacilli with many pus cells. November 14, 1931, trichomonads discovered. Quinine insufflation as in preceding cases and 15 gr. capsules given patient, to be introduced in the vagina each night. November 21, no discharge, no trichomonads. Quinine insufflation. November 28, no discharge, no trichomonads. Quinine insufflation. December 5, vagina clean, no discharge. Quinine insufflation. January 5, 1932, no discharge, no trichomonads. Patient dismissed.

CASE 5.—E. W., aged twenty-four, first seen August 3, 1931, with leucorrhea, odor and burning. Endocervix cauterized. November 17, 1931, trichomonads found. Quinine insufflation and capsules at home for one week. November 28, 1931, no trichomonads. Quinine insufflation. December 19, 1931, postmenstrual slide showed no trichomonads and no discharge. Quinine insufflation. January 2, 1932, no trichomonads.

CASE 6.—F. K., aged fifty, first admitted August 8, 1931, for vaginal itch, burning. Menopause twelve years ago. Slides showed trichomonads four-plus and sugar in urine. Treated with sodium bicarbonate and sodium perborate. August 15, 1931, no improvement. September 18, 1931, instillation of 10 per cent mercurochrome daily, no improvement. November 7, 1931, no improvement, quinine used. November 22, 1931, no discharge; itch still present. November 28, 1931, quinine insufflation. No trichomonads found; itch still present. Urine still showed sugar and patient presently under care of medical department for diabetes mellitus.

CASE 7.—N. M., aged twenty-one, first seen November 17, 1931, complaining of discharge, burning and itching. Date of last menstrual period was November 16, 1931. Claims to have had burning and itching for six months, and had been treated before by someone else with mercurochrome and vaginal tampons. Trichomonads four-plus. Quinine insufflation. November 19, 1931, nonmotile trichomonads. Quinine insufflation. November 20, 1931, trichomonads still present and nonmotile. November 21, 1931, no discharge and no trichomonads found. Patient has not reported since.

COMMENT

While the number of cases is very small and no positive conclusion should be drawn from the treatment of these few instances of Trichomonas vaginitis, still the results so far are so good that we have no hesitancy in inviting the medical profession to try it.

CONCLUSIONS

Seven cases of Trichomonas vaginitis were reported, six of the patients having received miscellaneous treatment with no improvement. All seven improved clinically and microscopically under the use of quinine treatment.*

GOLDSMITH BUILDING.

*At present we have five additional cases under treatment with apparent equally good results.

BLOOD CHEMISTRY STUDIES OF NORMAL NEWBORN INFANTS

A PRELIMINARY COMMUNICATION

I. BLOOD SUGAR ESTIMATIONS

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THE results of our studies of the blood sugar levels in women suffering from true toxemia* in the last trimester of pregnancy agreed with the findings of Titus.[1] From this fact we were led to the premise that the offspring of these women must necessarily have a hypoglycemia and that hypoglycemia must often be the cause of neonatal death. We therefore began to give, empirically, 5 to 6 gm. of glucose in 50 per cent solution to the babies of toxemic mothers, administering it by syringe into the umbilical vein. These babies seemed to do better and the mor-

*We use this expression to differentiate from nephritis.

tality rate of twenty babies, born alive, of toxemic or eclamptic mothers was 5 per cent, the only one which died being a seven months' child with a torn tentorium.

TABLE 1

MOTHER	MOTHER'S BLOOD	BABY'S BLOOD (CORD)
1	131	103
2	90	74 } Twins
		78 }
3	121	80
4	101	87
5	101	93
6	85	70
7	105	101
8	106	104
9	91	112
10	91	75
11	74	80
12	104	101
13	140	129
14	70	72
15	114	76
16	107	109
17	76	63
18	85	101
19	80	60
20	80	78
21	80	81
22	121	76
23	72	60
24	90	96
25	129	96
26	109	63
27	80	68
28	104	90
29	109	116
30	80	67
31	122	107
32	115	109
33	72	71
34	85	80
35	87	70
36	112	104
37	87	74
38	114	104
39	96	74
40	78	72
41	107	87
42	110	100
43	80	70
44	110	110
45	140	126
46	132	140
47	80	80
48	160	170
49	90	100
50	100	50
	102 average	90.4 average

The next step seemed to be a quantitative estimation of the glucose in the blood of infants from toxemic mothers. Preliminary to this, however, we undertook a comparative study of the glucose in the bloods of normal mothers and their babies, at delivery.

TECHNIC

Before the cord was cut, a needle was inserted into the umbilical vein several inches from the umbilicus and the blood withdrawn and placed immediately into an oxalated tube.[2] In some instances, however, the blood was taken directly from the maternal end of the cord, after it had been cut. Simultaneously blood was drawn from the median basilic vein of the mother. The Haskins, Osgood modification of the Schaffer microcopper method of blood sugar estimation was used routinely in all tests. No blood was allowed to stand more than two hours[3] before the sodium tunstate-sulphuric acid filtrate was made.

It will be seen (Table I) that the blood sugar levels in this small series fall into the same general range as do adult levels. Also that in most instances, the babies' blood sugar levels were relatively the same or below those of their mothers. This would indicate that if the mother suffers from hypoglycemia the fetus probably does.

As Stander[4] points out, and as our work has confirmed, the toxemic mother has a lowered alkali reserve. Hence, it is reasonable to suppose that her fetus will also have a lowered alkali reserve. We are now studying the comparative alkali reserves of newborn babies and their mothers with relation to the blood sugar levels and will report our results later.

CONCLUSIONS

1. The majority of normal babies have blood sugar levels at birth relatively the same as, or below, those of their mothers.
2. It would appear that babies of mothers with hypoglycemia must of necessity have a hypoglycemia in the majority of instances.
3. The neonatal mortality of babies born of toxemic mothers can probably be decreased by the administration of glucose to these infants at birth.

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URETERONEPHRECTOMY DURING EARLY PREGNANCY

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THE surgeon is frequently called upon to operate during the course of a pregnancy. Most frequently the lesion demanding his attention is in the appendix, and next in order, the gall bladder, and then the thyroid gland. These will constitute over half of the operations of necessity during gestation. In the lesser group of cases will be found quite a variety of intraabdominal and extraabdominal surgical lesions, for which operations on the kidney constitute about 4 per cent of the whole, and roughly 10 per cent of the lesser miscellaneous group.

Schmidt[2] in 1915 collected 6 cases, 1 his own, in which nephrectomy had been performed during pregnancy, and in addition to Hartman's collected series of 30 cases reported in 1913, made a study of the entire group. In this group there were 2 maternal deaths, 3 spontaneous abortions, 1 induced abortion, 1 induced labor, and in 1 a dead fetus was extracted. Mussey and Crane[1] of the Mayo Clinic in 1927 reported a series of 370 operations of necessity performed during pregnancy over a period of ten years. In this series there were only 4 maternal deaths and 17 miscarriages. (Interestingly enough all 4 deaths followed operations on the appendix or gall bladder, and over a third of the miscarriages followed operations on the uterus (myomectomy) or on the ovary.) There were 14 operations performed on the kidney, of which only 2 were ureteronephrectomy. In this group there were no maternal deaths and only one miscarriage. They concluded that any operation can be performed prior to the fifth month of gestation without undue risk to the mother and child.

CASE REPORT

We wish to report a case where ureteronephrectomy was performed during the first month of pregnancy, without knowledge of the patient being pregnant.

A young white girl, aged nineteen, who said she was single, was referred to one of us (Dr. McKnight) complaining of excruciating attacks of left-sided pain. Her family history was of no importance. Menses began at twelve and had always been normal and regular. She stated that her last period was just over. Her past medical history was negative except for the usual diseases of childhood, and these attacks of pain coming on at irregular intervals for the past two years. It seemed that they would appear after fairly strenuous exercise such as dancing or vigorous walking. Two months before she was first seen she had a very severe attack of left-sided pain extending from the renal area downward and inward toward the bladder and vulva. Since then she has had attacks every few days. The pain was evidently acute, as it caused her to cry out and writhe in bed and frequently required large doses of morphine for relief. She noticed no blood in the urine; although there was some urinary frequency but no pain on voiding. For the past week she had been confined to bed under morphine and symptomatic treatment, but suffering nevertheless.

Examination revealed a well developed and nourished young white woman, weighing about 110 pounds. Her blood pressure was 100 systolic and 64 diastolic; pulse 100; temperature 99.6°. Examination was negative except for marked pain, tenderness, and rigidity over the left renal area extending downward and forward over the abdo-

men toward the bladder. Pelvic and rectal examination revealed no abnormality. Her urine contained a trace of albumin and many pus cells; hemoglobin was 70 per cent (Sahli); leucocytes 26,000; Wassermann negative and blood urea 15 mg. per 100 c.c. of blood.

She was taken to the hospital where cystoscopic examination and pyelograms were made by Dr. J. P. Kennedy. The urine from the right kidney was normal, and there was normal function; that from the left contained many pus cells, and this kidney showed about 50 per cent normal function. Pyelograms showed the right kidney perfectly normal in size and position. The left ureter showed an obstruction about 20 cm.

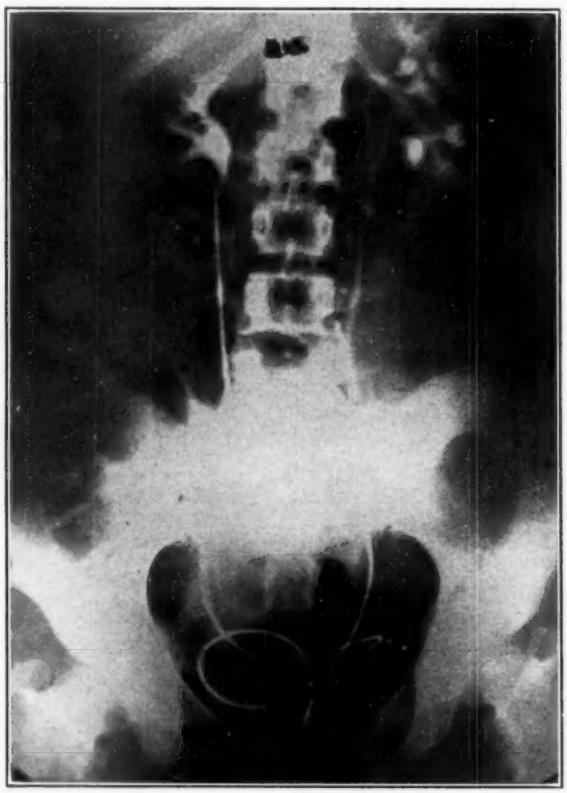

Fig. 1.—Ureteronephrectomy during early pregnancy.

above the vesical orifice. Injection of opaque medium was followed by exposure and at the point of bifurcation this ureter showed two well formed pelvices in one cortex. It was considerably larger than the right. Left nephrectomy and ureterectomy was decided upon and was performed by Dr. McKnight. The ureters were dissected out to a point about 3 cm. below the bifurcation and there ligated and cut. The kidney was about twice the normal size and had many adhesions about it, but was freed with little difficulty and removed. The patient made an uneventful recovery and was dismissed from the hospital the fifteenth postoperative day with the wound draining a minute amount of serum. Pathologic report was double ureters and pelvices, pyelonephrosis, multiple abscesses in the parenchyma of the kidney. A catheterized urine specimen two months subsequently showed only an occasional pus cell and was otherwise normal. She had complete relief of her symptoms and had gained several pounds in weight.

About four months after her operation she called for medical attention. On questioning her she stated that she had no special trouble, but "just wanted to see the doctor as she had been married two months before operation and was a month pregnant when operated upon." She stated that she had been married during a two- or three-day period when she was free from pain, and wanted to keep it a secret from her family. Examination revealed a five months' pregnancy. She was referred to Dr. Reid Patterson for obstetric care.

Studies at this time showed an entirely normal urine, hemoglobin 60 per cent (Sahli), 3,660,000 red blood cells, Wassermann negative and blood chemistry normal. Frequent urinalyses and blood pressure determinations showed that she had a normal period of gestation, toward the end of which the urine contained a little albumin and a few pus cells in a voided specimen. She entered labor at 7:00 o'clock the morning of May 10, 1930, eight months after operation. External examination revealed irregular uterine contractions, a breech presentation, and strong fetal heart sounds with a rate of 138. Vaginal examination at 10:30 A. M. revealed a rigid cervix, two finger dilatation, membranes intact, and a breech presentation. She was given 1/6 gr. of morphine sulphate and 1/200 gr. of hyoscine hydrobromide hypodermically to insure a comfortable first stage. She continued to make good progress and when the breech was well down on the perineum, a left episiotomy was done under ether anesthesia. At 1:10 P. M. she delivered herself of a normal baby boy weighing 2920 gm. The episiotomy was repaired in the usual manner and shortly afterwards the placenta was delivered intact. There were only about 25 c.c. of blood lost in this delivery. Pituitrin and ergot were given postpartum. She reacted nicely and was removed to her room in good condition. Recovery was uneventful, and she was dismissed from the hospital the seventh day. At this time her red cell count was 4,480,000, hemoglobin 65 per cent (Sahli), and a catheterized specimen of urine showed fairly numerous pus cells and a cloud of albumin. One month later a voided specimen was entirely negative except for an occasional pus cell. Her health is now excellent, blood pressure, blood counts and urinalysis are normal. She has gained about 15 pounds in weight and has no complaints.

COMMENT

From a study of the scattered single case reports in the literature of nephrectomy during pregnancy, from the reports of Schmidt and of Mussey and Crane, and from observations on our own case, it would seem that there is no cause for concern in doing renal surgery during early pregnancy, provided the remaining kidney is normal as to function and infection. Following operation in such a case, there is no reason why a patient should not continue through her period of gestation as though she had two perfectly functioning and normal kidneys. It is undoubtedly the better judgment to perform nephrectomy, rather than allow the pregnancy to continue in the presence of a unilateral pyelonephrosis, with marked diminution of function, in a congenitally abnormal kidney. Such a condition would certainly augment the possibility of a severe bilateral renal infection before term. It is our belief that there are absolutely no grounds for therapeutic abortion in cases of unilateral renal disease, where, in a nonpregnant woman renal surgery would be indicated.

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PROFESSIONAL BUILDING.

HYPERTROPHY OF THE CLITORIS: REPORT OF TWO CASES

LYMAN W. MASON, M.D., DENVER, COLO.

(From the Department of Obstetrics and Gynecology, University of Colorado School of Medicine)

THE first case, and the one serving as the basis for this report, was a schoolgirl aged seventeen years; height 64 inches; weight 125 pounds. She was seen in the Out-Patient Department of Gynecology of the University of Colorado Medical School, to which she had been referred by the medical department because of complaint of leucorrhea and pain in the right lower quadrant. The pain had no relation to her menstrual periods. Leucorrhea began about two years ago, and had increased slightly in amount since.

Past History.—Never any serious illnesses. Menstrual periods began at the age of twelve; frequency every twenty-eight days; duration four days; moderate flow; never any dysmenorrhea.

Patient's mother and an aunt stated that the patient had always enjoyed excellent general health; was robust; had developed normally in every respect, but that she was unduly reticent, and that she accomplished her schoolwork with considerable difficulty.

Family History.—Father and mother living and well, aged forty-three and forty-two respectively. One brother, nineteen, probably tuberculous. Three sisters, ages eleven, fourteen, and sixteen, all in excellent health. Other family history negative, except for one uncle who is at present a patient in a psychopathic hospital, suffering from epileptiform attacks, which he insists are due to masturbation in youth. Psychiatric diagnosis is unknown.

Physical Examination.—General examination entirely negative, except as noted below. Typical general feminine development and personality. Voice soft and pleasing. Normal hair development and distribution. Breasts well developed.

Abdominal examination elicited marked tenderness over McBurney's point, with some suggestion of rigidity of the right rectus. The pain complained of was attributed to occasional mild exacerbations of a low-grade chronic appendicitis.

External genitalia showed mature development. Hair growth abundant and of feminine distribution, except for a very thin line of it reaching to the umbilicus.

Labia majora normal. Labia minora were hypertrophied and redundant, hanging from a markedly hypertrophied clitoris, which was rigidly erected.

Vestibule negative. Urethral meatus normal. Hymen perforate and unruptured. There was a copious and constant secretion from the openings of both vestibular (Bartholin's) glands. Vagina negative. Cervix negative, except for a rather profuse secretion, entirely normal in appearance. No erosion.

Uterus normal in size, in good position and freely movable. Both ovaries were palpated; they were normally situated and were of normal shape and size. Tubes not felt. No pelvic abnormalities were found.

The measurements of the erected clitoris were length, 5 cm., width at the base, 1.75 cm., and length of glans, 1.75 cm.

Following the examination, the patient was questioned regarding any autoerotic practices. These she at first flatly denied, but further indirect questioning elicited the fact that she had frequently and continuously masturbated, by stimulation of the clitoris, beginning at the age of eight. She stated that about a year ago she stopped the practice. This last statement, however, is probably not true.

Chief interest in the case was directed to the clitoris, which appeared as in Fig. 1.

Before examination, and therefore before any stimulation of the genitalia, the clitoris was rigidly erected. Only after some time at a subsequent examination did it be-

come flaccid, and then not entirely so. (Fig. 2.) The slightest touch anywhere about the external genitalia caused it to become rigidly erect, the erection occurring, as in case of a penis, by pulsations synchronous with the heart beat. Voluntary contraction of the levator ani and perineal muscles increased its rigidity and direction of erection, also as in case of an erected penis.

The clitoris was extremely sensitive. At one time while measuring its dimensions, orgasm occurred at the slight touch and pressure of the small celluloid scale used. This was entirely local in its manifestations, that is, marked by spasmodic contractions of the levators and perineal and vaginal muscles only. This lack of more general response I believe to be due to past frequent masturbation, which had accustomed the patient to the attendant sensations.

Opportunity was subsequently afforded to examine this girl's mother and her three sisters. The external genitalia in all were entirely within normal limits with the exception of the oldest sister, aged sixteen, who presented a condition almost identical with the one reported here, with the exception that she had no complaint of leucorrhea, and

Fig. 1.

Fig. 2.

it was evident that the sensitivity of the organ was much less marked than in the case of her older sister. I am informed by a colleague, who has had under his care at various times two aunts and a female cousin of these girls, that there is nothing remarkable in the development of their clitori.

There are various pathologic processes which cause enlargement of the clitoris. However, in such cases as the one under consideration, presenting so marked a degree of "normal" hypertrophy, the condition is a congenital one, probably hereditary and probably a recessive characteristic. The mother stated that she had noticed that the clitori of these sisters were always larger than normal. When we consider that the clitoris is a homologue of the penis, with its muscular and erectile anatomy so similar, the wonder is not that marked hypertrophy sometimes occurs, but that it occurs so infrequently.

Frequent and long continued clitoris masturbation (and almost all masturbation in the female is of the clitoris) usually causes some hypertrophy, but never to any extent comparable with that seen in the present cases. The

leucorrhea complained of is, I think, physiologic for the conditions found, with the probably quite constant reflex stimulation of the cervical and vestibular glands.

Conditions such as these bring up interesting problems in treatment. One is often in doubt as to the proper course to pursue, or the proper advice to give. There is no doubt that a condition such as has been described is undesirable. However, it might be worse. It is necessary to take into consideration more than the small portion of anatomy involved. We must consider the individual in the light of her entire personality. This is true in all gynecologic problems, and it is all too often ignored.

Sex desire and gratification are largely a matter of the psyche, and we do little to increase our patients' physical and mental health by any procedure which removes the means for gratification but leaves the desire. These cases are more frequently than not proper ones for the consideration and treatment of the psychiatrist, or more happily the gynecologist who is psychiatrist enough to know when and how to treat the minds of his patients, and when to treat their genitalia. Much harm has been done in the past, and is still being done, by such operations as circumcision, clitoridectomy, etc., for such indications as masturbation and other complaints which are dependent more upon mental factors than upon anatomical states.

Dr. Franklin G. Ebaugh, of the Department of Psychiatry, saw and examined this patient in consultation. His report in part follows:

"Psychiatric examination revealed an average adolescent girl of the dull normal type. Her general reactions in the home, the school and the community appeared to be normal, and when closely questioned she did not show any unusual or abnormal preoccupations regarding sex and the condition of the vulva. Her heterosexual interests appear to be normal. She enjoys contacts with the opposite sex but has not been unduly erotic. Her interests are typically feminine and her physical development shows the usual secondary sexual characteristics, with normal menstrual function, hair distribution, development of the breasts, etc.

"Opinion on the basis of the above examination is that an operative procedure at the present time is not indicated and may actually do harm and lead to an emotional fixation on the part of the child to the anatomical condition present. I am of the opinion that her sexual development and activities will be normal. Of course, later on in life, conditions of a physiologic or psychologic type may warrant an operative procedure."

Appendectomy was advised, and the leucorrhea explained on a physiologic basis. Since it was not markedly profuse, no treatment was considered advisable at the present. The condition of the clitori in both cases was minimized, and nothing was advised concerning it, trusting that within a few years marriage will occur with establishment of normal heterosexual relations.

These cases are reported because of the medical interest of a rather unusual condition, and its occurrence in two members of one family; to emphasize the wisdom of considering such cases as much from a psychiatric as from a gynecologic standpoint, and to point out that ill-advised or hasty surgery is more likely to be harmful than beneficial.

707 Republic Building.

CYANOSIS OF THE NEWBORN*

Case Reports Showing Value of X-Ray As An Aid In Diagnosis

Edward H. Dennen, M.D., F.A.C.S., New York, N. Y.

ROENTGEN rays as an aid in diagnosis of cyanosis of the newborn should be used more frequently. Intracranial hemorrhage is often accepted as the most probable cause, but an x-ray picture may show that the trouble is in the chest. Thus the physician's responsibility is lightened, and the risk of lumbar puncture is avoided. In making a differential diagnosis, the simpler procedure should be used first as it may show that the other is not necessary. The presence of one of at least five other possible

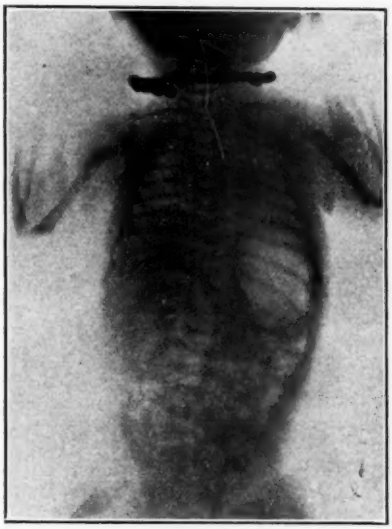

Fig. 1.

conditions may be established by the x-ray, and the treatment of each is quite different. Examples of these are shown in the following cases.

Case 1.—*Atelectasis:* Mrs. R. W., aged twenty-three, para i, gravida ii, was admitted to the Doctors Hospital on May 21, 1931. After thirteen hours of labor, she was delivered by low forceps to an L.O.A., of a female child weighing 6 pounds and 15 ounces. There was an initial asphyxia lasting fifteen minutes. During the next two hours the baby appeared normal. Then severe cyanotic attacks developed, occurring every ten or fifteen minutes. A physical examination did not reveal enough evidence on which to base a diagnosis. An x-ray of the chest (Fig. 1) taken when the baby was six hours old, showed nearly complete atelectasis of the left lung, and only partial expansion of the right lung. The cyanotic attacks continued for fifteen hours and then suddenly ceased. During this time carbon dioxide and oxygen were given through the Henderson machine with each attack.

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*Read before the Obstetrical and Gynecological Section of the N. Y. Academy of Medicine, December 22, 1931.

A second x-ray, taken four days later, showed normal expansion of both lungs. The baby was discharged well from the hospital on the fourteenth day, and is now seven months old.

CASE 2.—*Congenital Cardiac Lesion:* Mrs. M. C., para i, aged twenty-nine, was admitted to the Harbor Hospital, April 25, 1931. After seven hours of hard labor, she was delivered of a 6 pound boy by low forceps to an L.O.A. The baby was cyanotic for several hours after birth. There were several more attacks during the next three days, and cerebral hemorrhage was feared. Then for ten days the baby appeared well, but the attacks returned and were much worse.

The heart was found to be enlarged. This led to the suspected diagnosis of a congenital heart condition. The x-ray diagnosis was the same (Fig. 2). One week later the baby died, and on autopsy the diagnosis was confirmed. There were three chambers in the right heart; a rudimentary pulmonary artery, and a large patent foramen ovali.

Fig. 2.

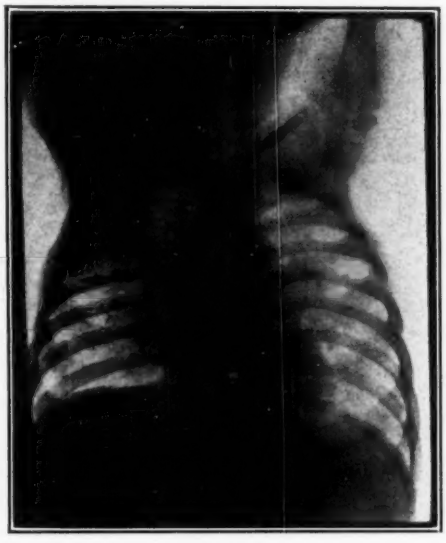

Fig. 3.

CASE 3.—*Pneumonia:* Mrs. R. S., aged thirty-four, para v, was admitted to Bellevue Hospital, August 17, 1931. She had nineteen hours of hard labor with an L.O.P. position. After a tentative trial with forceps, delivery was accomplished by version and breech extraction, and Piper forceps to the after-coming head. The baby weighed 8 pounds, and was markedly asphyxiated. The efforts at resuscitation were prolonged After using the Flagg and Drinker machines for an hour, the respirations were regular but labored.

During the next day, there were several cyanotic attacks. On the second day, the attacks were much worse. An x-ray picture of the chest was taken, but before the report was returned, a lumbar puncture was done, and 12 c.c. of clear spinal fluid, under moderately increased pressure were withdrawn. At this time, the diagnosis of severe intracranial injury, with extradural hemorrhage was considered probable. Later, the x-ray report showed consolidation of the upper lobe of the right lung, and a patchy consolidation around the right root (Fig. 3). Three days later the baby's condition was much improved, and on September 11, he was discharged in good condition.

CASE 4.—*Thymus:* Mrs. J. N., was admitted to the Polyclinic Hospital October 6, 1931. She was a para ii, twenty-six years old, at term, but not in labor. Her first child was delivered by cesarean section, because of a generally contracted pelvis, with a breech

presenting. The baby developed cyanotic attacks. The diagnosis was enlarged thymus. After x-ray therapy was given, the child recovered and is well today.

At this time, a 6 pound 6 ounce baby was delivered by elective cesarean section. There was marked initial apnea. The baby was finally made to breathe with the aid of the Flagg machine, but the respirations were shallow.

An x-ray picture showed an enlarged thymus. One x-ray treatment was given, but the baby died after seventeen hours. An autopsy was done. The brain was normal. There was a moderate amount of mucus in the air passages. The thymus was considerably smaller than its shadow appeared in the x-ray plate 14 hours earlier. The lungs showed early beginning pneumonia. The remainder of the autopsy was negative.

Although the diagnosis was not substantiated by the autopsy, the case serves to illustrate one of the possible causes of cyanosis, and the method of diagnosing it. There was considerable hesitancy about presenting this case, first because of the pathologist's

Fig. 4.

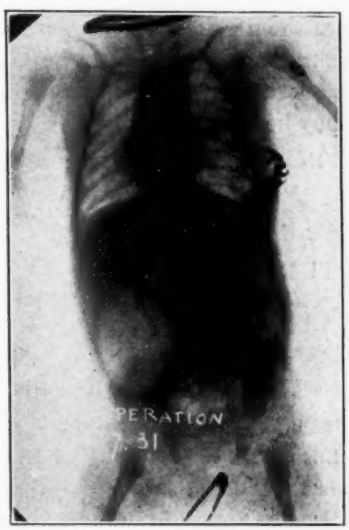

Fig. 5.

findings; and second, because of the discussion among authorities as to whether the thymus is really a pathologic entity in these cases.

Case 5.—*Diaphragmatic Hernia:* Mrs. M. S., para i, aged nineteen, a private patient of Dr. Hawks, was admitted to the Polyclinic Hospital August 4, 1931, in labor at term. She was delivered after eleven and one-half hours of labor because of the disappearance of the fetal heart, by mid forceps to an R.O.A. The baby weighed 6¼ pounds and was in good condition.

On the seventh day, the baby developed cyanotic attacks, with rapid and irregular respirations. The diagnosis of intracranial hemorrhage was accepted as most likely, and the condition was treated as such. The next day an x-ray of the chest was suggested, but the baby was considered too sick to be moved to the x-ray room.

The responsibility for this condition was place upon the physician by the father of the child because of the forceps delivery. Later, an x-ray picture was taken which showed a left diaphragmatic hernia, with the intestines in the left chest (Fig. 4). As her condition was steadily getting worse, the baby was operated upon successfully on the thirteenth day by Dr. Coryllos. The postoperative x-ray showed normal lung expansion but the heart had not yet returned to the left chest (Fig. 5). The baby was discharged well after six weeks, and is now in good health at four months of age.

All these cases of cyanosis in the delivery of which I had some part, occurred during a period of six months, showing to some extent the relative frequency of this condition. All were seen by consultants, and in only one was the correct diagnosis made before an x-ray picture was taken, showing the difficulty in making a diagnosis, and the value of x-ray aid.

Intracranial hemorrhage was not the primary diagnosis in all, but in the absence of other evidence, it had to be considered as a possibility. Although an autopsy may reveal a condition which relieves the doctor of the responsibility of intracranial hemorrhage, it also shows, in some instances, that had an x-ray picture been taken, and the indicated treatment been given, death might have been prevented. If no autopsy is obtained, the real cause is often not known, but the weight of medical opinion may force the doctor to sign the death certificate as intracranial hemorrhage. So both of these embarrassments may often be avoided by the early aid of a simple, flat x-ray picture of the chest, regardless of the baby's condition, or how sure one may be of his diagnosis.

133 East Eightieth Street.

RUPTURE OF A CORPUS LUTEUM AS A CAUSE OF ACUTE ABDOMINAL SYMPTOMS*

Case Reports

Waverly R. Payne, M.D., F.A.C.S., Newport News, Va.

During the past two years I have had occasion to operate on two instances of this condition, both being positively diagnosed by pathologists.

Case 1.—E. B., aged twenty-three, colored, married five years but never pregnant, called me on January 5, 1930, because of severe abdominal pains. Her past history was negative. Her periods were regular, every twenty-eight days, the last one ending one week previously. On several occasions she had had slight pains in the left lower quadrant, but never severe. On the occasion of the present attack during coitus she was seized with a sharp agonizing pain in the left lower quadrant, which radiated across the entire lower abdomen. She became nauseated but did not vomit. There was no vaginal bleeding. Examination revealed a well developed, and well nourished young Negro woman writhing in pain. Her temperature was normal, pulse 100, heart and lungs negative. The lower abdomen, especially on the left, was extremely tender and rigid. Morphine, ¼ grain was given, and an additional ⅙ grain before relief was obtained. Vaginal examination was deferred until the following morning at which time the patient was much more comfortable. She was still extremely tender to pressure, and had marked rigidity in the left lower quadrant. The perineum was firm. There was no bleeding or unusual discharge. The cervix was smooth, and normal in position. The uterus was slightly displaced, backward and to the right. The right ovary was palpable, and apparently normal in size. On the left there was marked tenderness in the region of the tube and ovary where a small soft mass was felt. Catheterized specimen of urine was negative. Wassermann negative. Hemoglobin 77 per cent, R.B.C. 3,776,000, W.B.C. 6,600, polys 51 per cent, small leucocytes 45 per cent, large leucocytes 3 per cent, eosinophiles 1 per cent. The diagnosis of chronic

*Read at a meeting of Warwick County Medical Society, January 14, 1932.

salpingitis with left ovarian cyst was considered most logical. The cause of the acute pain was not satisfactorily explained. The patient was advised to go to the hospital at the time of the acute attack, but desired to wait until the following morning. Next morning she was more comfortable, and her general condition better. She waited two days longer before entering the hospital. During this latter interval there was no improvement in her local condition.

Operation: Under spinal anesthesia the abdomen was opened and about 200 c.c. of old blood was found in the pelvic cavity. The right tube was chronically inflamed and adherent to the right ovary which was approximately normal in size. The left tube was chronically inflamed and adherent to the left ovary which was twice its normal size, and contained a large fresh corpus luteum body through which there was a rent 1 cm. in length. The appendix was somewhat congested. Both tubes, the left ovary, and appendix were removed.

Pathologic report (Dr. Sam Budd), was as follows: Chronic salpingitis, chronic cystic ovaritis with a large fresh ruptured corpus luteum body showing on the surface. This patient had an uneventful convalescence, and left the hospital on the tenth day.

CASE 2.—Miss M. V. R., aged thirty, clerk. On April 28, 1930, while at work she was seized with a rather severe sharp pain across the lower abdomen, which within a few hours became localized in the right lower quadrant. She was nauseated, and vomited once. Her past history revealed several attacks of tonsillitis, and several attacks of indigestion characterized by gas and belching. On several occasions she had noticed soreness in the region of the appendix. Her menstrual periods were usually regular every twenty-eight days, lasting five days, accompanied by pain on the first day. Her last period began three weeks previously. Physical examination revealed a normally developed and well nourished young woman. Her tonsils were infected. Heart, lungs, etc., negative. Temperature 98.2, pulse 80, blood pressure 120/80. Examination of the abdomen revealed marked tenderness, with rigidity over McBurney's area, extending rather deep into the pelvis. Rectoabdominal examination revealed the uterus moderately displaced backward. There was marked tenderness in the right lower quadrant. A small soft tender mass was felt just posterior and to the right of the uterus. Urine was negative, Wassermann negative, hemoglobin 83 per cent, R.B.C. 4,360,000, W.B.C. 8,400, polys 51 per cent, small leucocytes 46 per cent, eosinophiles 2 per cent, basophiles 1 per cent. The preoperative diagnosis was appendicitis, and cyst of the right ovary.

Operation: Under ether anesthesia a right rectus incision was made. The appendix was easily located. It was somewhat longer than normal, and presenting in the pelvis. There were a few old adhesions, otherwise no demonstrable pathology. It was removed. The uterus was normal in size and in second degree retroversion. The left ovary and tube were normal. The right ovary was enlarged to three times its normal size, and presented numerous cysts on its surface, one of which had ruptured. There was approximately 125 c.c. of blood in the culdesac. The right tube and ovary were removed.

Pathologic report (Dr. Beecroft), was as follows: Appendix and right tube normal. The right ovary measured 3.5 by 2 by 2 cm. The surface presented a wrinkled appearance. A small opening was noted at one end, and surrounding this the tissue was blood stained. The microscopic examination of this area showed a large corpus hemorrhagicum developing in the margin of which luteal cells were seen. Recovery was uneventful, and this patient left the hospital on the twelfth day.

COMMENT

In the two cases reported there was a sudden onset with definite evidence of intra-abdominal pathology. Neither of these cases exhibited significant changes in the blood picture.

MEDICAL ARTS BUILDING.

ENTRANCE OF LIPIODOL INTO OVARIAN AND OTHER VEINS DURING UTEROGRAPHY

JOHN CHARLES KILROE, B.A., M.D., AND ALFRED M. HELLMAN, B.A., M.D., F.A.C.S., NEW YORK, N. Y.

(From the First Gynecological Division Lennox Hill Hospital)

BELIEVING that the condition presented by the following case is still generally unknown, we herewith offer this report. No similar case report could be found in the literature up to 1932, and one of our largest clinics reported never to have seen such a case.

Fig. 1.—Roentgenogram taken directly after injection of lipiodol.

Mrs. M. N., age thirty, was born in Italy and has been in the United States for ten years. She has been married six years; has never been pregnant. Her menses started at 13, are regular, of the twenty-eight day type, and last six to seven days; the bleeding is scanty and there is no pain. For four years the menses have been becoming less frequent and more scanty. She came to the Lenox Hill Hospital Clinic because of this reduction in her menses, her seeming sterility, and complaining of some indefinite pain on the right side of the abdomen, low down.

Two examinations of the uterus and tubes by means of the injection of lipiodol into the uterine cavity demonstrated an apparent intravisation of lipiodol into the vessels of the uterine wall, and outlined both ovarian veins. This is easily seen from the accompanying pictures (Figs. 1 and 2). Bimanual examination is entirely neg-

ative, and no direct cause for the phenomenon is demonstrable in this patient. This finding is most unusual. Robin and Schapiro in the *New England Journal of Medicine* (Vol. 205, p. 380) showed a picture of this condition which they produced by injecting lipiodol into the extirpated uterus, using great pressure. In our case on the living subject no undue pressure was used, and the process was not at all painful.

Fig. 2.—Taken three minutes after injection of lipiodol.

Three theories for the production of this phenomenon are mentioned:

1. Injection under high pressure.

2. Injection after injury of the mucous membrane of the uterine wall, as with a curette.

3. Softening and permeability of the vessel walls.

Neither of the first two reasons are applicable to our case, and no undue softening or permeability of the vessel walls could be demonstrated unless the phenomenon herewith described demonstrates that such permeability of the vessels exists.

1114 Madison Avenue.
44 East 78th Street.

REPORT OF THE RESULTS AFTER TWELVE YEARS, IN A CASE OF URETEROVESICAL ANASTOMOSIS*

H. DAWSON FURNISS, M.D., NEW YORK, N. Y.

A. R., sixty-one years old, single. In August, 1919, was operated upon for large uterine fibroid. One week later developed incontinence of urine.

When first seen by me on October 15, 1919, examination revealed a vesicovaginal fistula ½ inch in diameter, situated just to the left of the median line, ¾ of an inch

Fig. 1.

posterior to the interureteric ridge. The left ureter drained into the vagina through a minute orifice high in the left vaginal fornix. Indigocarmine was eliminated strongly from the left as well as from the right ureter.

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*Presented at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, February 23, 1932.

On October 30, 1919, I implanted the left ureter into the bladder according to the technic published by me in the *American Journal of Obstetrics and Diseases of Women and Children*, 77: No. 1, 1918. On January 12, 1920, the vesicovaginal fistula was closed through the vagina. The convalescence from both operations was uneventful.

Since that time, except for hypertension, there has been no trouble. In September, 1927, her blood pressure was 250/150, and has kept at this figure since. On cystoscopy the implanted ureter appears as a minute orifice, that will admit a No. 6 catheter. Through it indigo carmine is eliminated as well as on the right, and in normal rhythm and force. On November 30, 1930, a pyeloureterogram was done. This shows only slight dilatation of the ureter, pelvis, and calyces. On January 27, 1932, phenolsulphonephthalein was injected intravenously; in seventy minutes 33 per cent was eliminated. The urine was pus free. Only a few hyaline casts and a trace of albumin were found.

Many of the ureterovesical anastomoses are followed by ureter stricture, hydroureter and hydronephrosis, often associated with infection. This successful outcome is reported as a stimulus to the performance of ureteral implantation in suitable cases.

54 East Sixty-Second Street.

AN INSTRUMENT TO OUTLINE THE PFANNENSTIEL INCISION

Sydney S. Schochet, M.D., and Julius E. Lackner, M.D.,
Chicago, Ill.

THE transverse or Pfannenstiel incision offers an excellent exposure for pelvic operations, lessens the occurrence of postoperative hernias, and obviates the ugly scar appearance so frequently seen after the low median incision.

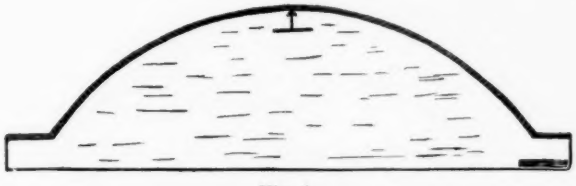

Fig. 1.

It appears to us that the reason there are not a large number of adherents to the Pfannenstiel incision in this country is due to the fact that it is frequently wrongly placed, and the curved transverse incision is not symmetrical with the result, that a poor exposure is obtained.

We have found that the apparent disadvantage of Pfannenstiel incision can be obviated if the skin is marked before the operation. For this purpose we have devised a metallic marker with a curve, whose radius is 12.5 cm. with an arrow to indicate the median line and a transverse mark to indicate that the curve is bisected.

The skin is marked with mercurochrome along this curve just within the line of pubic hair. The classical incision is then made along this marked curve.

55 East Washington Street.

A CASE IN WHICH SEVERAL FOREIGN BODIES WERE FOUND IN THE VAGINA OF A FEEBLE-MINDED PSEUDOHERMAPHRODITE*

DR. R. A. LIFVENDAHL, CHICAGO, ILL.

The history available was very inadequate because of the noncooperative attitude of this feeble-minded colored patient. Her only reason for coming to the clinic of Dr. Emil Ries was the presence of a foul smelling discharge. No statement was volunteered by her that any objects had been introduced by her until the vaginal examination, and then with considerable difficulty. The only significant fact obtained was that she had never menstruated.

The patient was short statured, colored, twenty-three years of age, with slightly prominent eyes but no other evidences of hyperthyroidism. The hair of the body had the typical male distribution and the chin was the site of a moderate growth of thin black short hair. The breasts were flat and of a male type. The heart, lungs, and abdomen were free from any abnormalities. Her voice was of a female tone.

Vaginal examination revealed a normally developed vulva and introitus. The clitoris was 3 cm. long and up to 2 cm. in diameter, had a well developed glans, and prepuce of corresponding size. No pus was found in the urethra or labial glands. The vagina admitted the index finger with moderate ease and when the latter had been introduced to a depth of 5 cm., numerous small metallic bodies were palpated. By manipulation a hexagonal shaped nut 1 cm. in diameter was removed, with two round metallic beadlike structures like the buttons of a shoe. After this she became restless and refused further examination at this time.

One week later she returned and at this time four more shoe buttons, two rubber balls, and the cap of a tooth paste tube were easily taken out with a small gall bladder scoop. A small cork, with its broad end directed upwards was removed from granulation tissue in the posterior fornix. Now she stated that all these objects had been inserted over a period of eight months. She denied having had intercourse at any time.

Bimanual examination, after these foreign bodies had been removed, demonstrated a vagina of normal length but no cervix, body of uterus, or appendages could be identified.

REPORT OF A CASE OF VELAMENTOUS INSERTION OF THE CORD WITH RUPTURE, AND SUBSEQUENT DEATH OF FETUS IN UTERUS†

DR. HENRY B. BOLEY, BROOKLYN, N. Y.

S. K., white, aged twenty years, last menstrual period January 10, 1931, expected date of confinement, October 17, 1931. General physical examination negative, except for a systolic murmur at the apex. The uterus was in good position and enlarged to about a ten weeks' pregnancy. No bony abnormalities were noted. Blood pressure was 110/70. Urine was negative.

Her prenatal course was uneventful except for occasional mild headaches, some pyrosis and slight edema of the legs. Blood pressure varied between 110 and

*Described before meeting of the Chicago Gynecological Society, March 18, 1932.
†Presented at meeting of the Brooklyn Gynecological Society, May 6, 1932.

118 systolic except on one occasion when it reached 130, but promptly returned to normal. Urine examinations were repeatedly negative. Patient experienced quickening on June 13.

On October 13 at 3:30 A.M., the patient began having labor pains, mild and occurring about every twenty minutes. At 4:30 A.M., there was a large gush of water followed immediately by profuse bleeding and many large clots. She was then admitted to the Jewish Hospital. At this time, she had only moderate vaginal bleeding and pains were slight and occurring every ten to fifteen minutes. Patient's pulse and temperature were normal. She had good color and the blood pressure was 140/90. The uterus was at full term, not tense, with fetus in R.O.A. position. The fetal heart could not be heard. The presenting part was floating and the cervix just admitted a tip of a finger. Voided urine specimen at this time was contaminated with blood. A catheterized specimen was negative. It was felt at this time that death of the fetus and the hemorrhage was due to a rupture of a velamentous vessel.

Pains ceased shortly after admission but a slight steady bleeding continued. Blood pressure at 2 P.M. was 150/100. On October 14 at 1 A.M., the pains started up again and from then on labor progressed normally and rapidly and resulted in a spontaneous delivery of a male stillborn at 9:50 A.M. The fetus weighed 6 pounds and the skull showed signs of beginning maceration. The placenta was then expressed complete with membranes. No abnormal bleeding followed. The patient had an uneventful postpartum course.

The placenta was 20 cm. in diameter. The cord was inserted into the membranes about three inches from the placental margin; from this point, the vessel diverged in the membranes to the margins of the placenta. There was a rupture of one of the vessels at a point midway in its course to the margin of the placenta.

REPORT OF A CASE OF YELLOW ATROPHY OF THE LIVER IN THE LATTER PART OF PREGNANCY, WITH RECOVERY*

DRS. CAMERON DUNCAN AND GLEN R. MACLACHLAN, BROOKLYN, N. Y.

Mrs. N. B., colored, aged twenty-nine, was admitted to Kings County Hospital October 27, 1931. She had been seen one week previous in the prenatal clinic, and was advised then to enter the hospital at once for complete examination and observation because of previous cesarean section.

The past history was entirely negative. There were two previous pregnancies, one ten years before, terminating in a forceps delivery followed by six weeks' hospitalization, and one five years ago by cesarean section. The indications for both were not known. Menstruation normal, the last menstrual period February 12, 1931, the calculated date November 19, 1931. The pregnancy to date had been uneventful except for moderate nausea and vomiting during the first four months.

There was present a slight thyroid enlargement and the abdomen was enlarged to the size of an eight and a half months' pregnancy, with an upper midline scar from the previous cesarean section. Weight 155 pounds, height five feet, normal blood pressure and pelvic measurements. The laboratory data on admission, including urinalyisis, blood count and blood chemistry, was normal.

On October 31, four days after admission, the patient was taken ill, first with chills, then nausea, vomiting, headache, a rise in temperature to 102° and pulse to 120. Physical examination negative except for moderate injection of the pharynx and a

*Presented at meeting of the Brooklyn Gynecological Society, May 6, 1932.

mild nasal catarrh. A diagnosis of grippe was made. The urine at this time showed 2-plus albumin; otherwise negative. Blood count: 4,096,000 red blood cells, 15,300 white blood cells, 80 per cent hemoglobin and 75 per cent polynuclear cells. A blood chemistry showed urea 35, creatinin 1.3, sugar 114. The following day the patient appeared acutely ill, had a fainting spell and the temperature reached 101°, with the pulse 128 and weak. At this time cardiac stimulation was commenced.

On November 2, slight jaundice appeared for the first time. She complained of severe headache and pain in the chest and back. She was still nauseated and not retaining food or fluids. At this time, tenderness below the right costal arch developed. A surgical consultation on this date was negative for gall bladder disease or appendicitis. For the first time, casts appeared in the urine, the albumin was increased but the blood count remained as on previous examination. The urine was negative for leucin and tyrosin crystals. The following day, November 3, the patient was still more deeply jaundiced, the severe headache, nausea and vomiting persisted, and she complained of generalized muscular aches and pains. A blood count on this date showed 3,500,000 red blood cells, 8,600 white blood cells, 75 per cent hemoglobin and 75 per cent polynuclear cells. The coagulation time was six minutes. The icteric index was 78 and the Vanderberg test showed a direct immediate positive reaction. The upper liver margin was at the third rib, and the lower border three fingers below the costal margin. Opinion, toxic hepatitis. The fetal heart had been heard and appeared normal up to this time, but disappeared November 4.

On the afternoon of November 5, the patient went into labor and had an easy, spontaneous delivery of a seven-pound macerated fetus. Nitrous oxide was given for five minutes. The next day, the patient was symptomatically improved. The increased liver dullness previously noted was lessened. The spleen was not palpable. The blood pressure was normal, as was the urine except for a faint trace of albumin. The blood chemistry showed urea 168, creatinin 2, sugar 145. Red blood cells 2,350,000; hemoglobin 25 per cent; white blood cells 30,000; polynuclears 66; lymphocytes 30; monocytes 3; eosinophils 1; degenerative index 89 per cent; microcytosis two-plus; macrocytes one-plus; anisocytosis three-plus; reticulated cells 2 per cent. On November 6, there was pronounced weakness and muscular pains. The jaundice remained but the liver was progressively getting smaller. A blood chemistry at this time showed urea 158, creatinin 3, sugar 133, icteric index 113, Vanderberg direct immediate positive reaction. On November 8, the patient was clear mentally in contrast to her previous persistently apathetic state but the intake of food still caused vomiting. The jaundice was definitely less and the blood chemistry practically the same as previously reported. On November 9, a 400 c.c. blood transfusion was given.

The condition gradually improved but a second transfusion of 500 c.c. was given. The urine report was still negative for leucin and tyrosin. A third transfusion of 500 c.c. was given on November 16. On this date, there were 2,500,000 red blood cells; 9,700 white blood cells, 65 per cent hemoglobin, and 73 per cent polynuclear cells. From this time on, the patient made rapid recovery, had no subjective complaints and on November 23 was allowed out of bed. On November 25, twenty-six days after the onset of the illness, she was discharged in good condition. Treatment had included cardiac stimulation intermittently as indications arose, and repeated clyses of saline, and infusions of glucose, saline, and calcium gluconate, as well as the three blood transfusions previously mentioned.

A blood culture taken during the period of acute illness was sterile. At the time of discharge from the hospital her blood count showed 4,000,000 red blood cells and 70 per cent hemoglobin and a normal urinalysis and blood chemistry. The diagnosis was "acute hepatitis with partial acute yellow atrophy."

DISCUSSION

DR. SAMUEL A. WOLFE.—Cases of yellow atrophy of the liver are known to recover after persuing a mild subacute course. Mallory of Boston has reported a series of this type, clinically simulating catarrhal jaundice. Regeneration and fibrosis occurs, and the liver ultimately assumes the gross characteristics of typical Laennec's cirrhosis.

In the case reported, the diagnosis of acute yellow atrophy requires further confirmation. The abrupt onset with chill and high temperature is rather atypical. The sudden hemolysis shown by a rapid drop in the number of the red blood corpuscles and in hemoglobin are indicative of a hemolytic anemia. The overloading of the circulation with hemoglobin derivatives easily account for the enlargement of the liver reported early in the disease. The blood chemistry in both hemolytic jaundice and acute yellow atrophy are somewhat similar. Retention of urea, uric acid, and creatinin, occurs in both.

The Van den Bergh reaction and the icteric index as reported appear in hemolytic jaundice. The high icteric index is indicative of obstruction of the biliary radicles due to overload of pigment. In the light of these facts the diagnosis of acute yellow atrophy does not appear completely substantiated.

DR. CAMERON DUNCAN.—The fact that leucin and tyrosin crystals were not found is not a constant factor in acute yellow atrophy, as Hunter, in an analysis of 23 cases found 9 that had neither leucin nor tyrosin, 10 cases with both leucin and tyrosin, 3 cases that had tyrosin alone, and one case with leucin alone.

Kottlors: The Treatment of Postoperative Urinary Retention. Zentralbl. f. Gynäk. 54: 2530, 1930.

Most of the commonly employed drugs such as urotropin, pilocarpin, calcium acetate, ammonium chloride, etc., do not have a direct influence on urinary retention, but derive their effect from psychic action. Obviously retention is due to one of two causes; muscle deficiency, or sphincter spasm. A postoperative patient is anxious to spare her abdominal muscle and, therefore, will not try to micturate. In this group, the personality of the physician is an important item. Sphincter spasm has been treated with antispasmodic drugs of the atropine group without much success. The writer claims that a rectal infusion of 50 c.c. of 2 per cent novocaine solution will be effective within one hour in the large majority of cases. Of 31 postoperative patients 84 per cent responded well to this therapy, urinating within an hour following the application. Even cases of urinary retention following radical Wertheim operation were favorably influenced.

WILLIAM F. MENGERT.

Errata

On page 939 of the December issue the word Standard's in the twenty-first line from the bottom of the page should read Stander's.

On page 899 of the December issue, the second paragraph should read:

It is therefore evident that the theory of an increase of CO_2 as a cause of slowing of the fetal heart should be discarded (instead of discovered).

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

Meeting of March 8, 1932

The following papers were presented:

Epithelial Regeneration in the Uterine Glands and on the Surface of the Uterus. Dr. G. N. Papanicolaou. (See page 30.)

An Analysis of the Menstrual Changes in Tuberculous Women. Dr. E. M. Jameson. (See page 22.)

BROOKLYN GYNECOLOGICAL SOCIETY

Meeting of May 6, 1932

The following papers were presented:

Report of a Case of Velamentous Insertion of the Cord With Rupture, and Subsequent Death of Fetus in Uterus. Dr. H. B. Boley. (See page 156.)

Report of a Case of Yellow Atrophy of the Liver in the Latter Part of Pregnancy, With Recovery. Drs. C. Duncan and G. R. MacLachlan. (See page 157.)

Congenital Pneumonia of the Stillborn and the Newborn. Dr. J. Kaldor. (See page 113.)

The Complications of Radium Therapy in Gynecology. Dr. G. G. Ward. (See page 1.)

CHICAGO GYNECOLOGICAL SOCIETY

Meeting of February 19, 1932

The following papers were presented:

The Technic of Radiation Therapy in Uterine Carcinomas. Dr. H. Schmitz. (See page 10.)

Internal Rotation of the Fetal Head, From the Viewpoint of Comparative Obstetrics. Dr. L. Rudolph and Dr. A. C. Ivy. (See page 74.)

CHICAGO GYNECOLOGICAL SOCIETY

Meeting of March 18, 1932

The following papers were presented:

A Case in Which Several Foreign Bodies Were Found in the Vagina of a Feeble-Minded Pseudohermaphrodite. Dr. R. A. Lifvendahl. (See page 156.)

Report of a Case of Ovarian Embryoma. Dr. P. J. Sarma. (See page 51.)

Some Urologic Complications in the Female. Dr. G. Kolischer. (See page 128.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

Endometrium

Hofbauer, J.: Concerning the Etiology of Hyperplasia of the Endometrium, Surg. Gynec. Obst. **52**: 222, 1931.

The etiology of hyperplasia of the endometrium presents a problem which is still inadequately understood. Several writers have recently expressed the view that in all probability an unrecognized endocrine factor is concerned in the etiology of this condition, i. e., in view of the present knowledge of the nature of hormones in the blood and in the urine, great caution should be exercised in drawing conclusions from positive or negative findings in them.

Hyperplasia may reasonably be regarded as the manifestation of an overactivity of the anterior pituitary lobe. This conclusion, that an outside factor represents the primary cause of the disease, was reached when guinea pigs which were treated parenterally with derivatives of the anterior pituitary, produced conditions in the uterine mucosa, as well as in the ovaries, which were practically identical with those observed in endometrial hyperplasia in women. This obtained so long as the ovaries were preserved but when they had been removed, the process was limited to the basal portion of the endometrium. This conclusion is corroborated by the clinical experience that the condition commonly recurs after repeated curettage.

The question arises as to whether the anterior lobe of the pituitary registers its effect on the uterine mucosa directly or through the agency of the ovary. The author's observations indicate that the internal secretion of the ovary is essential for the changes occurring in the upper part of the uterine mucosa—"the functionalis," while the basal layer is under the control of the anterior pituitary lobe, as judged by the response of this structure to repeated pituitary administration in ovariectomized animals.

WM. C. HENSKE.

Burch, John C., Williams, W. L., and Cunningham, R. S.: The Etiology of Endometrial Hyperplasia, Surg. Gynec. Obst. **53**: 338, 1931.

This is a careful histologic survey of numerous specimens of the human endometrium at various stages of the menstrual cycle. The findings from this material were compared with the histologic changes of the endometria of spayed mice which had been injected with extracts of estrin and corpus luteum and with a combination of the two. From these comparisons it was possible to gain an idea of the histologic manifestations which the various hormones produced.

Sections from 28 cases of Swiss cheese hyperplasia were studied in the light of these comparisons. Two typical cases of Swiss cheese hyperplasia from which both the uteri and ovaries were available for study were observed, in both a follicular cyst was present. Fluid from these cysts was injected into spayed mice and rats and the endometria from these animals were compared with that from the human uteri.

It was found that both estrin and the corpus luteum hormone produce a definite and characteristic reaction on the endometrium.

It is possible in cases in which mixed effects are obtained to determine by means of histologic study which of the hormones is predominant.

The histologic appearances of the endometrium obtained from cases of Swiss cheese hyperplasia are very similar to those found in animals which have been injected with extracts of placenta.

Material obtained from the follicle cysts of human cases of hyperplasia when injected into mice and rats, produced estrus. The changes in the uterus of each case were similar in many respects to those found in the uterus of the experimental animals receiving the fluid from that case. WM. C. HENSKE.

Adler, K.: The Clinical Manifestations of Glandular Hyperplasia of the Endometrium, Monatschr. f. Geburtsh. u. Gynäk. **90:** 340, 1932.

The etiology of granular hyperplasia of the endometrium is not clear. In most cases, there are enlarged ovaries with one or more follicle cysts and in the majority of cases, no corpus luteum is present. Adler studied 67 cases of endometrial hyperplasia from the clinical point of view. Most of the patients were more than thirty-six years of age (68.7 per cent). The next most frequent group was between fifteen and twenty-five years. The most prominent symptom was uterine bleeding and this varied considerably in type. In the majority of cases the bleeding consisted of an increased flow during the menses but the intervals between the periods were prolonged. In most cases the uterus was enlarged and this was observed in the very young patients as well as in the older ones. Almost all of the patients were nulliparas. The uterus was generally softened and the cervical canal offered no resistance to mechanical dilatation. During the preclimacteric period and the menopause, the enlarged uterus was usually associated with fibroids. The latter showed a special tendency to increased growth during the menopause. Zondek has shown that at the onset of the menopause there is an increased amount of follicular in the blood and urine. It is therefore conceivable that the hyperplasia in the climacteric may be due to an excess of the proliferation hormone.

During the reproductive years there is a special tendency toward hyperplasia among nulliparas; for of the 17 women between fifteen and thirty-five years of age, 14 had never borne children. On the other hand, among the 45 women who had hyperplasia during the preclimacteric and the climacteric only 5 were nulliparas.

The treatment for women over forty years of age is simple. After curettement is performed and the diagnosis made, roentgen-ray therapy should be employed. In women past the menopause curettage alone usually suffices. In young women, a curettement is necessary for a diagnosis and it generally produces a temporary cure. However, the condition usually recurs. Hysterectomy is never necessary.

J. P. GREENHILL.

Reinhart, H. L., and Moore, R. A.: Tuberculous Endometritis, J. Lab. & Clin. Med. **14:** 413, 1929.

The incidence of tuberculosis of the uterus is not as common as is often assumed. Primary tuberculosis of the female genital tract is extremely rare, in fact the exact modus operandi of infection has never been proved. Most tuberculous infections of the genital tract are secondary. Infection is usually transmitted through the blood stream (metastatic) and the original lesion is most frequently in the lung or bronchial lymph nodes. Metastatic lymphatic infection to the genitals is rare. The uterus being an organ which is constantly contracting, the lymph flow through that organ is so active that bacilli are not permitted to remain in one place long enough to develop a lesion. With menstruation the uterus performs a "physiologic curettage" by shedding itself. This physiologic function together with the menstrual congestion prevents chronic infection with ordinary bacteria, and this same factor is probably operative in the case of tuberculosis.

Reinhart and Moore state that the macroscopic appearance of tuberculous tubes and uteri in 75 per cent of cases cannot be distinguished from infectious lesions due to other organisms. Clinically, there is no pathognomonic symptom of tuberculous infection of the genital tract. The authors report two cases, worthy of note, the one with secondary tuberculosis of uterus and tubes, secondary probably to pulmonary tuberculosis, and the second a tuberculosis superimposed upon an atrophic fibrosis uteri. The authors conclude that there is a marked variation in the reported frequency of tuberculous lesions in the female genital tract; that the physiologic activities of various portions of the female genital tract may be responsible for variation in resistance to tuberculous infection and that tuberculosis of the uterus is more frequently superimposed upon a pathologic than a normal organ. W. B. SERBIN.

Miscellaneous

Nakawaga, J.: Prolapse of the Uterus and Constitution. Japanese J. Obst. & Gynec. **14**: 106, 1931.

At the Gynecological Institute of the Kyoto Imperial University prolapse of the uterus was observed during the last nine years in 1.18 per cent of all the patients and prolapse of both the uterus and vagina in 2.57 per cent. More cases were found in young women than is generally believed. Parity played a rôle in the following order of frequency: quadripara, primipara, tertipara, sextipara and quintipara. There was a relatively large number of prolapses among multiparas because the incidence among them was 4.55 per cent. An asthenic constitution was observed in 34.1 per cent of the cases, and tuberculosis was noted in 36.4 per cent. The author believes that prolapse of the uterus is caused by an abnormal constitution and that there is a close relationship between prolapse and tuberculosis. The latter leads to a deterioration of the constitution.

J. P. GREENHILL.

Wislocki and Snyder: On the Experimental Production of Superfetation. Bull. Johns Hopkins Hosp. **49**: 103, 1931.

On June 12 a healthy, mature female rabbit was mated at 4:50 P.M. On June 16 at 12:15 P.M. this animal received 8 c.c. of anterior lobe extract intravenously. On the same day, at 4:30 P.M. they inseminated the animal artificially. On June 17, at 9:15 P.M., the animal was killed and autopsied.

The observation recorded demonstrated the possibility of successfully fertilizing a second set of ova. The living blastocysts had not prevented a second set of ova from becoming fertilized. Nor had the changes occurring supposedly in ovaries, tubes and uterus, after fertilization of the first set, prevented a second set of normal ova from being discharged and becoming fertilized. The present experiment fails to support the concept of the primacy of the ovum. The ova do not apparently exert an inhibitory influence upon ovulation, fertilization and maturation of a second set of ova.

This demonstration of the possibility of superfetation opens a number of avenues of investigation. It will be interesting to determine the fate of the second set of fertilized ova in the presence of the initial set of blastocysts. Will the period of transit through the tubes become altered? Will the spacing of the first set of ova or the reaction of the endometrium following their implantation prevent successful implantation of the second set? Does the time of implantation of the ovum depend upon the stage of development of the ovum or upon the condition of the endometrium? These and other questions can be answered by further similar experiments. C. O. MALAND.

Items

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

At the meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons held at French Lick Springs on September 12, 1932, a resolution was passed, taking note of the "increasing necessity for the determination and certification of specialists in the various branches of medicine," to the effect that in the future candidates for Fellowship in this Association who profess to be specialists in obstetrics and/or gynecology be required to be Diplomates of the American Board of Obstetrics and Gynecology. Official action of the Executive Council is necessary for any special exceptions to this regulation.

At the recent meeting and examination of the American Board of Obstetrics and Gynecology held in Los Angeles, December 7th, the following applicants were approved for certification:

Max J. Abramson, Los Angeles, Calif.
Theodore W. Adams, Portland, Oregon.
T. Floyd Bell, San Francisco, Calif.
Warren Watson Bell, Seattle, Wash.
R. Glenn Craig, San Francisco, Calif.
Roy E. Fallas, Los Angeles, Calif.
Frederic Fluhmann, San Francisco, Calif.
George B. Greenbaum, Los Angeles, Calif.
John Curtis Irwin, Los Angeles, Calif.
O. Donovan Johnson, Los Angeles, Calif.
Emil J. Krahulik, Los Angeles, Calif.
Fred Lindenberg, Los Angeles, Calif.
Frederic M. Loomis, Oakland, Calif.
Clarence W. Page, Berkeley, Calif.
Albert V. Pettit, San Francisco, Calif.
Henry M. Rooney, Los Angeles, Calif.
Moses H. Ross, Los Angeles, Calif.
Charles S. Salisbury, Los Angeles, Calif.
Henry N. Shaw, Los Angeles, Calif.
John W. Sherrick, Oakland, Calif.
Alson A. Shufelt, San Jose, Calif.
Gordon Grahame Thompson, Seattle, Wash.
William B. Thompson, Los Angeles, Calif.
Leon J. Tiber, Los Angeles, Calif.
Albert M. Vollmer, San Francisco, Calif.
John Vruwink, Los Angeles, Calif.

Three additional candidates were conditioned and four candidates failed of certification.

The next written examination and review of case histories will be held in cities throughout this country and Canada, where there are Diplomates who may be empowered to conduct the examination, on April 1, 1933.

The next general, clinical examination is to be held in Milwaukee on Tuesday, June 13, 1933, immediately preceding the annual session of the American Medical Association. Reduced railroad rates will apply.

Early application is requested from those desiring to qualify for these examinations. For further information and application blanks address Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.